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VALUE OF CONVALESCENT SERUM FOR THE PREVENTION OF COMMON CONTAGIOUS DISEASES OF CHILDREN

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AND

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This study was carried out on the entire children's service of the Fifth Avenue Hospital from June 11, 1931, until July 1, 1934. During this period 1,717 children were admitted to the pediatric department, which occupies the whole second floor of the building and contains sixty-three beds (fig. 1). Of these sixty-three beds, nine are in separate rooms, nineteen in cubiculized wards and thirty-five in open wards. Even in the open wards, the beds are 6½ feet (1.98 meters) apart and are separated by glass partitions 8 feet (2.4 meters) high. Both the partitions and the cubicles end 3¼ feet (0.99 meter) below the ceiling. The whole floor is divided into four equal units: two for the medical service, one for the surgical service and one for the outpatient department. As the same doctors and nurses were in direct communication with all four wings, which are connected with corridors, from the point of view of this study we considered the whole floor, with the exception of the outpatient department, as one unit. We excluded the outpatient department because the patients there had only short contact with the nurses and doctors and no contact at all with the patients in the wards. Many of the children from the wards came into intimate association with each other on the open terraces, where all who were not too sick had the advantage of the open air.

In order to determine correctly the value of convalescent serum in the prophylaxis of a specific contagious disease, one must consider the following questions:

1. How long and how intensive is the child's contact with the original patient?

2. Is the source patient at the stage of contagion in which he spreads infection very readily?

3. What is the age of the child who is exposed to the contagious disease?

From the Pediatric Service of Fifth Avenue Hospital, Dr. Frederic Bartlett, Director.

4. Is the exposed child in all probability immune to the contagious disease, as proved in the case of diphtheria by a negative Schick test, in the case of scarlet fever by a negative Dick test and in the case of other communicable diseases, for which there are no susceptibility tests, by the fact that the child has had the disease in question?

5. The consequence of mild exposure to a contagious disease in a hospital ward is almost unpredictable. Therefore, are the control patients, who have had apparently the same exposure as the patients to whom convalescent serum is given, observed at the same time?

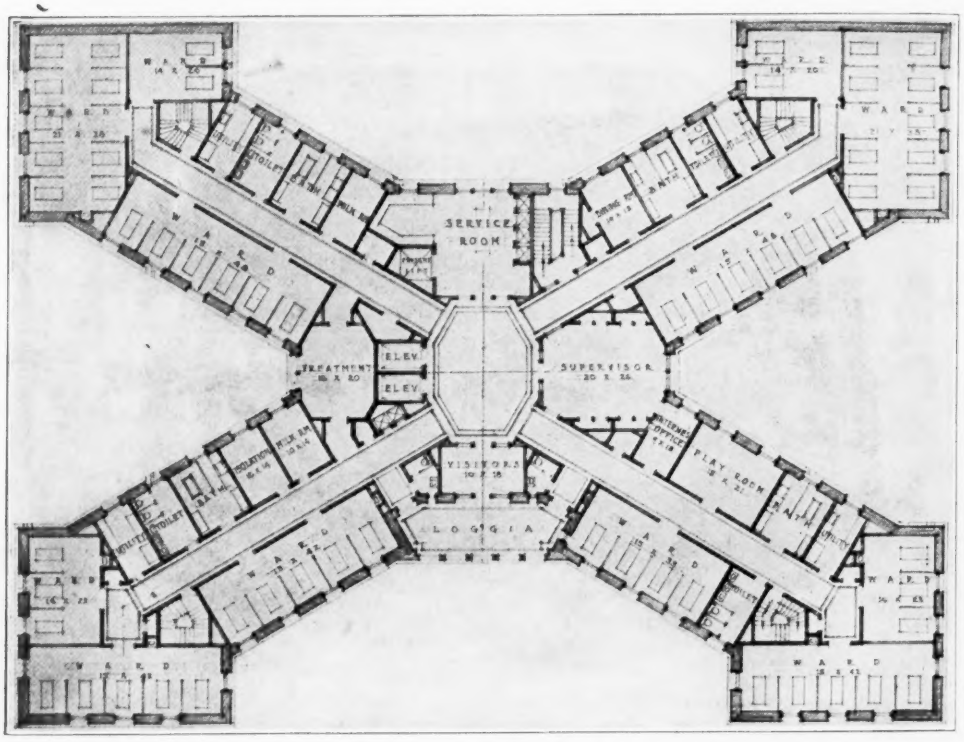

Fig. 1.—Plan of the children's floor.

PERSONAL OBSERVATIONS

Our own three years of experience in the prevention of contagious diseases furnishes enough data to show that these five points are essential in the correct evaluation of the benefit obtained from the use of the convalescent human blood serum.

1. *Length and Intensity of Exposure.*—As soon as a patient with a contagious disease was discovered in our service, the diagnostician of the department of health was called, and the patient was removed from the hospital as soon as possible. However, no quarantine was placed

on the wards; the admission and discharge of patients continued without interruption. Of twenty-nine original cases of contagious disease occurring at different times, only six produced secondary cases; therefore, it is safe to assume that exposure in the other twenty-three instances was either not long enough or not intensive enough to produce secondary cases. This is a remarkable record when one considers that no "aseptic technic" was used in our service. We handled our patients according to the average routine of a general hospital. In deciding which patient was to be treated and which one kept as a control, we first eliminated those who had had the specific disease, or who were immune to it, and made the rest of the ward population alternately controls or treated patients, considering the relation of their beds to the bed of the first patient. Exceptions were made of private patients and critically ill children. When we ran out of serum or, occasionally, when immunization would have had to be done on Sundays or holidays, we made the patients controls.

2. *Stage of the Disease of the Source Patient.*—Most of our source patients presented an early stage of the contagious disease when admitted to the hospital. Definite diagnosis could not be made at first, but symptoms developed while they were in the hospital. In some cases the diagnosis was made so early and the patient removed so quickly that no secondary case developed. Therefore, although the source patients presented different degrees of risk for the ward population, we may consider all of them as presenting a more or less early stage of the disease.

3. *Age of the Population of Our Service.*—Because children during the first few months of life have an inherited resistance to most common contagious diseases and because they become susceptible to these diseases at different ages, the age levels in the ward population modify in a definite way the tendency of the disease to spread. It is obvious that if all the children are over 10 years of age there is less danger of measles sweeping through the ward than if the majority of the children are under 5 years. This is true not only for measles but for other diseases, since a higher percentage of children over 10 are immune to the common contagious diseases of childhood either because they already have had the disease or because they have escaped it owing to their acquired resistance. Tables 1 and 2, together with figures 2 and 3, show the curve of immunity for the various contagious diseases at different age levels, as judged by the past history. The statistics on which these curves are based were compiled from our own material, collected during three years from 1,576 hospital patients. We did not use all the 1,717 children for obtaining these figures because only 1,576 of them had reliable histories of contagious disease.

TABLE 1.—*Frequency of Different Contagious Diseases of Childhood on the Basis of 1,576 Histories*

Age in Years	Total Number	Measles		German Measles		Chickenpox		Scarlet Fever		Whooping Cough		Mumps		Diphtheria	
		Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
0 to 1	246	8	3.2	..	...	3	1.2	..	...	7	2.8	..	....	..	...
1 to 2	244	44	18.0	..	...	19	7.8	..	...	25	10.2	3	1.2	1	0.4
2 to 3	155	46	29.7	2	1.3	25	16.1	2	1.3	26	16.8	11	7.1	..	...
3 to 4	125	48	38.4	2	1.6	23	18.4	3	2.4	19	15.2	11	8.8	2	1.6
4 to 5	98	49	50.0	..	...	20	20.4	3	3.1	29	29.6	6	6.1	1	1.0
5 to 6	107	64	59.8	5	4.7	36	33.6	5	4.7	35	32.7	15	14.0	6	5.6
6 to 7	138	93	67.4	..	...	49	35.5	9	6.5	51	36.9	20	14.5	10	7.2
7 to 8	94	63	67.0	2	2.1	30	31.9	8	8.5	38	40.4	18	19.1	4	4.2
8 to 9	89	67	75.2	2	2.2	42	47.0	5	5.6	32	36.0	23	25.9	5	5.6
9 to 10	84	65	77.4	2	2.4	30	35.7	7	8.3	35	41.7	16	19.1	10	11.9
10 to 11	88	75	85.2	3	3.4	40	45.4	11	12.5	41	46.6	17	19.3	5	5.7
11 to 12	72	50	69.4	2	2.8	24	33.3	6	8.3	34	47.2	8	11.1	5	6.9
12 to 13	36	29	80.5	1	2.77	14	38.9	4	11.1	17	47.2	8	22.2	2	5.5
All ages	1,576	701	44.5	21	1.33	355	22.5	63	4.0	389	24.7	156	9.9	51	3.2

From table 1 it may be seen that the frequency of common contagious diseases is directly in the following order: (1) measles; (2) whooping cough; (3) chickenpox; (4) mumps; (5) scarlet fever; (6) diphtheria; (7) German measles.

From table 2 and figure 3 can be seen not only the frequency of negative Dick and Schick reactions but the proportion of the children who received immunization against diphtheria. It is worthy of note that 29 per cent of the children were immune to diphtheria without being artificially immunized. This group of children very likely became immune naturally by subclinical disease or by contact with carriers of

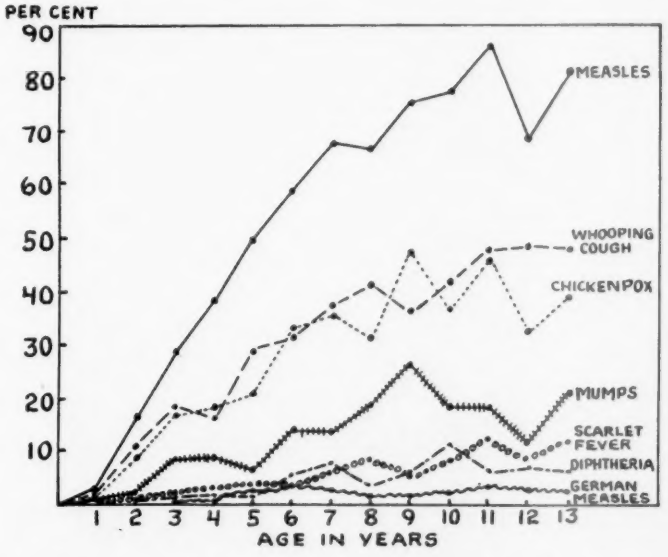

Fig. 2.—Chart showing the frequency of different contagious diseases among children.

diphtheria. Of course, in the first year of the child's life, immunity transferred from the mother must also be considered.

4. *Unsuitability of Immune Children for Testing the Value of Convalescent Serum.*—In the case of diphtheria and scarlet fever, the children with negative Schick and Dick reactions had to be eliminated from our groups. With the rest of the diseases, we had to rely on histories of contagious disease. These, of course, are not as reliable as biologic tests, but, as a whole, they served our purpose satisfactorily. Only presumably nonimmune children were used for prophylaxis with convalescent serum and for control purposes. Table 2 and figure 3 show the frequency of positive Schick and Dick reactions among the patients in the wards.

TABLE 2.—*Frequency of Positive Schick and Dick Reactions Among Patients of the Children's Service of the Fifth Avenue Hospital*

Age in Years	Total Number of Schick Tests	Positive Schick Reactions		Negative Schick Reactions		Total Number of Dick Tests	Positive Dick Reactions		Negative Dick Reactions		Total Number with History of Diphtheria Immunization	Diphtheria Immunization Done		Diphtheria Immunization Not Done	
		Number	Per Cent	Number	Per Cent		Number	Per Cent	Number	Per Cent		Number	Per Cent	Number	Per Cent
0 to 1	216	77	35.6	139	64.4	222	50	22.5	172	77.5	246	12	4.9	234	95.1
1 to 2	203	80	39.4	123	60.6	210	70	33.3	140	66.7	224	74	33.0	150	67.1
2 to 3	142	69	48.6	73	51.4	140	58	41.4	82	58.6	155	59	38.1	96	61.9
3 to 4	117	49	41.9	68	58.1	118	50	42.4	68	57.6	125	47	37.6	78	62.4
4 to 5	89	32	35.9	57	64.1	88	30	34.0	58	66.0	98	32	32.6	66	67.4
5 to 6	97	37	38.1	60	62.9	94	33	35.1	61	64.9	107	46	43.0	61	56.0
6 to 7	122	50	41.0	72	59.0	123	46	37.4	77	62.6	138	66	47.8	72	62.2
7 to 8	96	31	32.3	65	67.7	88	16	18.2	72	81.8	94	46	49.0	48	51.0
8 to 9	77	18	23.4	59	76.6	78	13	16.7	65	83.7	89	44	49.7	45	50.5
9 to 10	73	19	26.0	54	74.0	77	17	22.1	60	77.9	84	38	45.2	46	64.8
10 to 11	87	25	28.5	62	71.5	85	15	17.6	70	82.4	98	47	48.0	51	52.0
11 to 12	70	20	28.8	50	71.2	70	14	20.0	56	80.0	72	27	37.5	45	62.5
12 to 13	31	3	9.7	28	90.3	31	4	12.9	27	87.1	36	22	61.1	14	38.9
All ages	1,420	510	36.0	910	64.0	1,424	416	29.2	1,008	70.8	1,566	560	35.8	1,006	64.2

5. *Necessity of Using Control Cases.*—Since of the original twenty-nine cases of contagious diseases only six produced secondary ones, it is obvious that if we had given convalescent serum to all the ward population the lack of cross-infections in twenty-three instances would have been attributed wrongly to the protective effect of the serum. However, because we had a number of controls who did not present secondary cases, we knew that the exposure was either not intensive enough or not long enough and that the convalescent serum probably was not responsible for checking the spread of the disease. The lack of controls explains why the results of the various authors were so utterly different from one another.

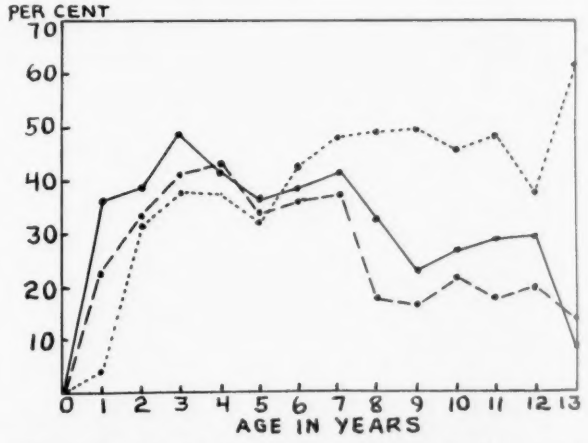

Fig. 3.—Chart showing the frequency of positive Dick and Schick reactions and of a history of immunization against diphtheria. The black line indicates positive Schick, and the short dashes, positive Dick, reactions. The dotted lines indicate immunizations against diphtheria.

REVIEW OF THE LITERATURE

Next we are going to analyze the results in the literature on the prophylactic use of convalescent serum against common contagious diseases of childhood and compare them with our own results. Because the articles on all these diseases except measles are few, we have tried to cover the complete literature in our tables. However we are limiting ourselves to articles on measles which deal with controlled experiments.

From table 3 it can be seen that to our knowledge there are eight articles published on the use of convalescent serum to prevent whooping cough. Some of these articles report on only one patient. Only two of the authors used controls. The frequency of cross-infections varied from 0 to 100 per cent. To us this means that the exposure of the immunized patients must have varied a great deal. The fact that Lewis and Barenberg reported 100 per cent failure with the use of whole blood

TABLE 3.—*Reports of Use of Convalescent Serum for Prophylaxis Against Whooping Cough*

No.	Author	Treated Patients			Controls			Dose of Serum	Comment
		Total	Number of Cross-Infections	Percentage of Cross-Infections	Total	Number of Cross-Infections	Percentage of Cross-Infections		
1.	Battley, F.: Arch. Pediat. **46**: 673, 1931.....	2	..	..	..	..	..	.....	
2.	Debré, R.: Bull. Acad. de méd., Paris **89**: 348 (March 13) 1923	40	9	22	..	..	..	2-3 cc.	Pooled serum, collected 4 weeks after the disease, used
3.	Debré, R.; Broca, R., and Bertrand, J.: Arch. de méd. d. enf. **27**: 157 (March) 1924	79	14	17	..	..	..	.....	
4.	Gautier, P.: Arch. de méd. d. enf. **28**: 801 (Dec.) 1925	1	..	..	..	..	..	.....	Protection lasted for several weeks
5.	Gillot, V.: Bull. Acad. de méd., Paris **93**: 176 (Feb. 10) 1925	10	..	..	..	..	..	2-5 cc.	Whole adult blood (6 patients with no history of whooping cough given injections of blood)
6.	Jundell, I.: Acta pædiat. **15**: 1, 1933.....	10	2	20	..	..	..	30-40 cc.	Injections of adult serum given in catarrhal stage
7.	Lewis, J. M., and Barenberg, L. H.: New York State J. Med. **33**: 97 (Jan. 15) 1933	6	6	100	11	11	100	30 cc.	Whole blood used; disease was milder in treated patients
8.	Jones, L. T., and Kittredge, E.: Women's M. J. **35**: 277 (Oct.) 1928	15	6	40	8	6	75	5-20 cc.	Adult blood used
9.	Kereszturi, C.; Hauptman, D., and Park, W.: Not published before	96	..	..	90	..	..	5-15 cc.	

both among their treated patients and among their control patients is significant even though they reported only about seventeen cases. Their findings make one pessimistic about the value of convalescent serum as a prophylactic against whooping cough. We have used a greater number of treated and untreated patients than any other worker. However, the fact that we did not observe cross-infections in either group renders it impossible for us to pass judgment on the value of this method.

There is also very little literature on the use of convalescent serum to prevent mumps. Of eight articles published on the subject, only three dealt with both treated and control patients. The rate of cross-infection again varied from 0 to 100 per cent. It is interesting to note that Hess, Lewis and Barenberg, who made their studies in the same orphan asylum at different times, reported entirely different results. This again proves that without studying control and treated patients at the same time one cannot estimate correctly the risk which the population of a ward faces in different outbreaks of a contagious disease. On one occasion in our own experience, the control group showed an incidence of cross-infection of 2.8 per cent whereas the treated patients showed none. On two other occasions, neither among the treated patients nor among the controls were secondary cases found.

We think that there is reason to hope that convalescent serum will give at least relative immunity to mumps. However, the proper dosage of the serum and the limit of time within which its administration is effective are not known.

The literature on the use of convalescent serum to prevent chickenpox is inconclusive because the authors who reported a sufficiently large group of cases did not have any controls. During our three years of study we had two occasions on which to study the effect of convalescent serum against chickenpox. In the first outbreak of chickenpox, neither the treated patients nor the controls showed secondary cases. In the second outbreak, however, we found an incidence of cross-infection of 1.5 per cent among the controls and of 15 per cent among the treated patients. The convalescent serum was taken from patients from 6 to 17 years old, nine months after the onset of chickenpox. In our experience convalescent serum was of no value as a prophylactic against chickenpox. In patients so treated the disease was not even appreciably modified.

Table 6 shows that four articles were found in the literature describing the use of convalescent serum prophylactically against scarlet fever. Two of these deal with large groups of children. Meader had 450 treated patients and 321 controls. All the authors seemed to have fairly good results with the serum. The frequency of cross-infection among the treated patients varied from 0 to 5 per cent, whereas in the two series having controls the incidence among the controls was from 12.8

TABLE 4.—*Reports of Use of Convalescent Serum for Prophylaxis Against Mumps*

No.	Author	Treated Patients: Total	Treated Patients: Number of Cross-Infections	Treated Patients: Percentage of Cross-Infections	Controls: Total	Controls: Number of Cross-Infections	Controls: Percentage of Cross-Infections	Dose of Serum	Comment
1.	Barenberg, L. H., and Ostroff, J.: Am. J. Dis. Child. **42**: 1109 (Nov.) 1931	55	8	14	125	49	38	12 cc.	In 11 cases 12 cc. of adult blood given; in 44 cases 12 cc. of convalescent blood given
2.	Cambessédès, H.: Ann. d'hyg. **11**: 83 (Feb.) 1933	184	1	0.5	..	4	..	10-20 cc. (children) 10-40 (adults)	In institutions results better than at home
3.	Gunn, W.: Brit. M. J. **1**: 183 (Jan. 30) 1932.....	21	3	14	22	5	22	5-15 cc.	Most patients exposed 1 to 5 days
4.	Hess, A. F.: Am. J. Dis. Child. **10**: 98 (Aug.) 1915	17	..	..	117	44	38	6-8 cc.	Whole blood used; immune children excluded
5	Lewis, J. M., and Barenberg, L. H.: New York State J. Med. **33**: 97 (Jan. 15) 1933	11	11	100	..	..	..	12 cc.	Whole blood; author concluded dose too small
6.	Regan, J. C.: J. A. M. A. **84**: 279 (Jan. 24) 1925...	70	1	1.4	..	..	..	3 cc.	
7.	Zeligs, M.: J. Pediat. **1**: 727 (Dec.) 1932.....	44	..	..	..	..	..	5 cc.	
8.	Skrotzky, A. I.: Odessky M. J. **4**: 8, 1929.....	179	2	1	..	..	..	5-15 cc.	
9.	Kereszturi, C.; Hauptman, D, and Park, W.: Not published before	17 42	.. ..	.. ..	36 51	1 ..	2.8 ..	5-7 cc. 7-15 cc.	4 hours' to 4 days' exposure ¼ to 1½ days' exposure

TABLE 5.—*Reports of Use of Convalescent Serum for Prophylaxis Against Chickenpox*

No.	Author	Treated Patients: Total	Treated Patients: Number of Cross-Infections	Treated Patients: Percentage of Cross-Infections	Controls: Total	Controls: Number of Cross-Infections	Controls: Percentage of Cross-Infections	Dose of Serum	Comment
1.	Blackfan, K. D.; Peterson, M. F., and Conroy, F. C.: Ohio State M. J. **19**: 97 (Feb.) 1923	42	7	17	..	..	..	5 cc.	Less than 5 days' exposure
2.	Gordon, J. E., and Meader, F. M.: J. A. M. A. **93**: 2013 (Dec. 28) 1929	162	32	19	81	55	68	10-15 cc.	Convalescent serum must be taken within 3 months after the disease
3.	Gunn, W.: Brit. M. J. **1**: 183 (Jan. 30) 1932.....	43	10	23	..	..	50	5-15 cc.	Exposure 1 to 6 days
4.	Lewis, J. M., and Barenberg, L. H.: New York State J. Med. **33**: 97 (Jan. 15) 1933	8	0	0	..	..	..	40 cc.	Adult serum
		5	5	100	..	..	..	30 cc.	Whole blood serum
5.	Mitchell, A. G., and Ravenel, S. F.: Arch. Pediat. **42**: 709 (Nov.) 1925	68	3	4.4	1	1	100	2-10 cc.	Exposure, 1 to 7 days; serum 11 months old in few cases
		22	1	4.5					
6.	Weech, A. A.: J. A. M. A. **82**: 1245 (April 19) 1924	9	1	11	..	..	..	3-4.5 cc.	1 to 6 days' exposure
7.	Kereszturi, C.; Hauptman, D., and Park, W.: Not published before	14	0	0	18	0	0	5-7 cc.	6 to 8 hours' exposure
		33	5	15	62	1	1.5	5-15 cc.	12 to 38 hours' exposure

TABLE 6.—*Reports of Use of Convalescent Serum for Prophylaxis Against Scarlet Fever*

No.	Author	Treated Patients			Controls			Dose of Serum	Comment
		Total	Number of Cross-Infections	Percentage of Cross-Infections	Total	Number of Cross-Infections	Percentage of Cross-Infections		
1.	Meader, F. M.: J. A. M. A. **94**: 622 (March 1) 1930	450	13	2.9	321	41	12.8	7.5 cc.	Convalescent blood taken within 1 year; immunity lasted 3 to 4 weeks
2.	Zikowsky, J.: Wien. klin. Wchnschr. **41**: 1408 (Oct. 4) 1928	79	4	5	5	1	20	10 cc.	
3.	Neff, F. C.: Arch. Pediat. **39**: 250 (April) 1922....	25	..	0	..	..	..	15-30 cc.	Immediate injection after exposure
4.	Degkwitz, R.: München. med. Wchnschr. **69**: 955 (June 30) 1922	509	3	0.6	..	..	..	5-10 cc.	
5.	Kereszturi, C.; Hauptman, D., and Park, W.: Not published before	38	..	0	37	..	0	5-15 cc.	

to 20 per cent. In our three years of experience we had only thirty-eight patients with positive Dick reactions, to whom we gave serum prophylactically from four hours to four days after exposure. At the same time we watched thirty-seven control patients with positive Dick reactions. No cross-infection was noted in either group; therefore, we were unable to collect data on the protective value of convalescent serum against scarlet fever.

We did not find any evidence in the literature indicating that convalescent serum ever was used for prophylactic purposes against German measles. We tried it on twenty exposed patients in the hospital. In none of them did German measles develop. However, twenty-six control patients similarly exposed and watched also failed to present secondary cases.

One can see a great contrast between the meager literature on the prophylactic use of convalescent serum to prevent German measles, chickenpox, whooping cough, scarlet fever and mumps and the abundant literature on its use to prevent measles. In table 7 we selected those articles which describe the use of convalescent serum, not adult serum or whole blood, and which report cases of control patients also.

On looking over our results and those of other investigators who have used convalescent serum prophylactically against measles, one can see clearly that the serum decreases the number of cross-infections. Without the use of serum, the rate of cross-infections varies from 25 to 100 per cent; if serum treatment is given, the rate of infection varies from 0 to 49 per cent. From table 7 one also can see that the dosage of serum given varied from 2.5 to 30 cc. If one realizes that not only the dosage and potency of the serum but the length and intensity of exposure before and after the serum was given varied considerably, one can understand why the results of different authors, and even our own results in different outbreaks, are so different. It is hard to compare our results with the findings of others for another reason. We were very careful to exclude the children who had had the disease already and to whom exposure meant no risk. On the other hand, not all the authors took care to do this, and some of them even did not mention whether they excluded the nonsusceptible children. However, all the workers have agreed that the early use of convalescent serum prevents measles in the majority of cases and makes it almost universally a milder disease when complete suppression does not occur.

SUMMARY AND CONCLUSIONS

For the past three years convalescent serum has been used prophylactically without quarantine against measles, German measles, chickenpox, whooping cough, scarlet fever and mumps in the children's service of the Fifth Avenue Hospital.

The total number of children admitted during this period was 1,717.

TABLE 7.—*Reports of Use of Convalescent Serum Against Measles*

No.	Author	Treated Patients: Total	Treated Patients: Number of Cross-Infections	Treated Patients: Percentage of Cross-Infections	Controls: Total	Controls: Number of Cross-Infections	Controls: Percentage of Cross-Infections	Dose of Serum	Comment
1.	Blackfan, K. D.; Peterson, M. F., and Conroy, F. C.: Ohio State M. J. **19**: 97 (Feb.) 1933	84	11	13	4	4	100	5 cc.	The earlier the serum is given the better the result
2.	Ferry, N. S.: Am. J. Dis. Child. **37**: 573 (March) 1929	85	22	26	127	40	31.5	5 cc.	
3.	Gunn, W.: Lancet **2**: 690 (Oct. 6) 1928.....	69	3	4	23	18	78	3-5 cc.	
4.	Heymann, K. G., and Bussel, R.: Deutsche med. Wchnschr. **57**: 747 (May 1) 1931	35	0	0	31	8	25	20-30 cc.	1. Adult blood used 2. Convalescent blood used
5.	Lewis, J. M., and Barenberg, L. H.: New York State J. Med. **33**: 97 (Jan. 15) 1933	66	16	24	23	23	100	6 cc.	
6.	Lichtenstein: Acta pædiat. **9**: 77, 1929.....	93	46	49	39	22	59	3-30 cc.	Larger doses, better results
7.	Morales, E. G.: Am. J. Dis. Child. **39**: 1214 (June) 1930	120	18	15	183	149	82	4-6 cc.	
8.	Warwick, W.: Canad. Pub. Health J. **20**: 597, 1929	75	6	8	2	2	100	6-10 cc.	2 children had temperature of 101 F. and lacrimation; 3 had otitis media
9.	Weaver, G., and Crooks, T. T.: J. A. M. A. **82**: 204 (Jan. 19) 1924	48	4	8	9	9	100	5-10 cc.	
10.	Wesselhoeft, C., and Gordon, F.; New England J. Med. **198**: 752 (May 24) 1928	51	14	27	25	25	100	5 cc.	
11.	Zingher, A.: J. A. M. A. **82**: 1180 (April 12) 1924	58	23	39	33	10	30	2-5-7.5 cc.	
12.	Kereszturi, C.; Hauptman, D., and Park, W.: Not published before	4	..	..	4	..	..		
		16	..	..	26	3	11		
		26	1	4	1	..	..		
		22	1	4	2	1	50		
		34	2	5	44	15	34		
		23	5	22	6	2	33		
	Total	125	9	7	83	21	25		

In cases of whooping cough, scarlet fever and German measles neither the controls nor the treated patients showed any cross-infections.

After one outbreak of mumps no second case was observed either among the treated or among the untreated patients. In a second outbreak, the controls showed an incidence of cross-infection of 2.8 per cent, whereas the treated patients showed none.

In one outbreak of chickenpox, no cross-infection was noted in either group. However, in the second outbreak, the treatment with serum seemed to fail. In this one, among the nontreated group the frequency of cross-infection was 1.5 per cent; among the treated group the rate of cross-infection was 15 per cent.

The different outbreaks of measles produced different amounts of cross-infection, the rate varying from 0 to 22 per cent among the treated patients and from 0 to 50 per cent among the controls. The average rate of cross-infection in the different outbreaks of measles was 7 per cent among the treated patients and 25 per cent among the controls.

We were unable to draw conclusions about the ideal time to collect convalescent serum or about the optimum prophylactic dose of the serum.

After three years of experience with the prophylactic use of convalescent serum we are convinced that unless control patients are observed simultaneously with treated patients one cannot determine the value of the convalescent serum.

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INFLUENCE OF A SPECIAL CEREAL MIXTURE ON INFANT DEVELOPMENT

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In October 1930 Tisdall, Drake and Brown [1] described a new cereal mixture which was rich in vitamins and mineral elements. They felt that the finely milled and refined products ordinarily used were deficient in many of the minerals and in all of the vitamins. Since the cereals form from 30 to 60 per cent of the daily caloric intake, the constituents of this component of the infants' diet deserve serious consideration. With this thought in mind they devised a cereal mixture that more nearly fulfilled the requirements for vitamins and minerals without disturbing the caloric value of the carbohydrate. By feeding groups of rats diets poor in a single vitamin, symptoms characteristic of deficiency of vitamins A, B, D and E, respectively, were produced. The addition of their cereal mixture to these experimental diets was sufficient to bring about clinical improvement in the animals.

The composition of this mixture is as follows: wheat meal (farina), 53 per cent; oatmeal, 15 per cent; bone meal, 2 per cent; dried brewer's yeast, 1 per cent, and alfalfa, 1 per cent.[2] An analysis of its mineral content gives the following results: total ash, 3.2 per cent; calcium, 0.78 per cent; phosphorus, 0.62 per cent; iron, 0.024 per cent, and copper, 0.0013 per cent.

In February 1932 Summerfeldt [3] reported on the results of the clinical use of this mixture at the Hospital for Sick Children in Toronto. Each group consisted of 21 children—15 boys and 6 girls ranging in age from 6 to 13 years—who were observed over a period of twenty-one weeks. For a ten week period 10 children in the first group were given 4 ounces (113.36 Gm.) of the special mixture in addition to the food

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Read before the Central States Pediatric Society, Sept. 23, 1933.

From St. Vincent's Infant and Maternity Hospital and the Department of Pediatrics, University of Illinois College of Medicine.

1. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: A New Cereal Mixture Containing Vitamins and Mineral Elements, Am. J. Dis. Child. **40**:791 (Oct.) 1930.

2. The cereal mixture used in this study is manufactured by Mead Johnson & Company and is called Mead's Cereal. Mead Johnson & Company furnished the cereal used in this problem.

3. Summerfeldt, Pearl: The Value of an Increased Supply of Vitamin B and Iron in the Diet of Children, Am. J. Dis. Child. **43**:284 (Feb.) 1932.

offered as a routine by the institution. A control group of 10 children received the usual cereals (farina, oatmeal, cornmeal and cut wheat). At the end of ten weeks, the diets of the groups were reversed.

An analysis of Summerfeldt's tables shows that those fed the special cereal gained from 2 to 3 times the expectancy, while the gain in weight of the control children in each instance coincided with the expectancy.

In August 1931 a study of the use of this product as compared with the cereals generally used was undertaken at St. Vincent's Infant and Maternity Hospital. This institution houses from 200 to 250 well children from birth to 3 years. In this study 136 children from 3 to 30 months of age were observed for periods varying from six weeks to one year. The children were divided into a special group of 70 and a control group of 66. Both groups were managed by the same nursing staff, and the diets differed only in the cereal given. The special group received only the mixture previously described, while the control group received the commonly used cereals as regular dietary components. All cereals were cooked with half milk and half water in a steam kettle for one-half hour and were fed as part of the morning meal. The quantity fed was dependent on the appetite of the child. No food was forced; additional helpings were given as desired. In this study every effort was made to conform as nearly as possible to the usual and approved method of feeding children in the private home.

Cow's milk with dextrimaltose formed the basis of the infants' diets. A regimen of orange juice and cod liver oil was begun during the first month. Cereal became a dietary component when the infant was 3 months old. Vegetables and soups were given at 5 months. Eggs and puddings were added during the ninth month. At 1 year the children were receiving a general diet which included whole boiled milk, cereals, vegetables, soups, puddings, toast, eggs, bacon, stewed fruits, cod liver oil and orange juice. Children of 15 months and more were fed in a common dining room with from 4 to 6 children at each table. Portions were served them and they fed themselves. The problem of anorexia does not exist in this institution.

In studies of the growth and development of children it has been repeatedly pointed out that age-weight tables alone are not a sufficient criterion. In reviewing various age-weight tables Emerson and Manny [4] emphasized their confused state and presented various tables giving different weights for the same height and age. Few such tabulations are available for the study of children under 3 years of age. Dublin and Gebhart [5] studied a group of 1,878 boys and 2,169 girls in an Italian dis-

4. Emerson, W. R. P., and Manny, F. A.: Tables of Average and Optimum Weight for Height, Arch. Pediat. **46**:382 (June) 1929.

5. Dublin, L. I., and Gebhart, J. G.: Height and Weight Tables Identify Undernourished Children, Am. J. Pub. Health **13**:920 (Nov.) 1923.

trict in New York to determine whether the diagnosis of malnutrition, as made by a competent pediatrician, coincided with that determined by height-weight tables. In their problem children whose weight fell from 7 to 10 per cent below the average for age and height were considered undernourished. The conclusion of the pediatrician, based on his examination of the child, did not coincide with that determined by comparison with height-weight-age tables alone. Blackfan [6] emphasized that in the study of increment of height or weight in childhood one should have consecutive measurements at successive ages. He pointed out that in studying groups the children should be as nearly alike as possible with regard to sex, color, social status, conditions of management, measurement and age.

In our study we had two groups of children in good health, living under as nearly ideal conditions as institutional life permitted. The children of both groups were from the same social strata, and the groups were about equally divided as to sex and color. (There were 4 Negro children in each group.) The diet and management were under the control of one person, and conditions for making periodic measurements and medical examinations were identical for both groups. All examinations and measurments were made by the same physician every two weeks during the twelve month period. The turnover at the institution is over 200 per cent per year and the results only in those children who were under observation for a period of more than six weeks are included in our tables.

In the study of the growth and the development of these two groups we attempted to select those anthropometric measurements most commonly used and those which in our opinion might give information of clinical value to the pediatrician. These included observations of weight, height, stem length or sitting height, circumference of the head, circumference of the chest and bicrestal diameter. Tabulations were made at two week intervals. Records were kept on the eruption of teeth and incidence of infection. Determinations of hemoglobin content were made once each month. Roentgenograms of the forearms for evidence of rickets or syphilitic changes in the bones were taken of all the children at the start and at the completion of the study.

OBSERVATIONS

Weight.—The weight of each child was taken between 9 and 10 a. m., after the morning bath. We used standard beam scales which were checked at three month intervals to avoid discrepancies between

6. Blackfan, K. D.: White House Conference on Child Health and Protection: Growth and Development of the Child: III. Nutrition, New York, Century Company, 1931.

those in the various wards. Group weight graphs were started when the child was 6 months old when the division into the two feeding groups was made. For the preceding six weeks the diet included all cereals, and if older children were included they had been on a diet containing the usual cereals for a longer time. Averages of the semimonthly weights of children from 6 to 30 months were used as the basis for the graph in figure 1. Figure 1, therefore, is a composite of the average

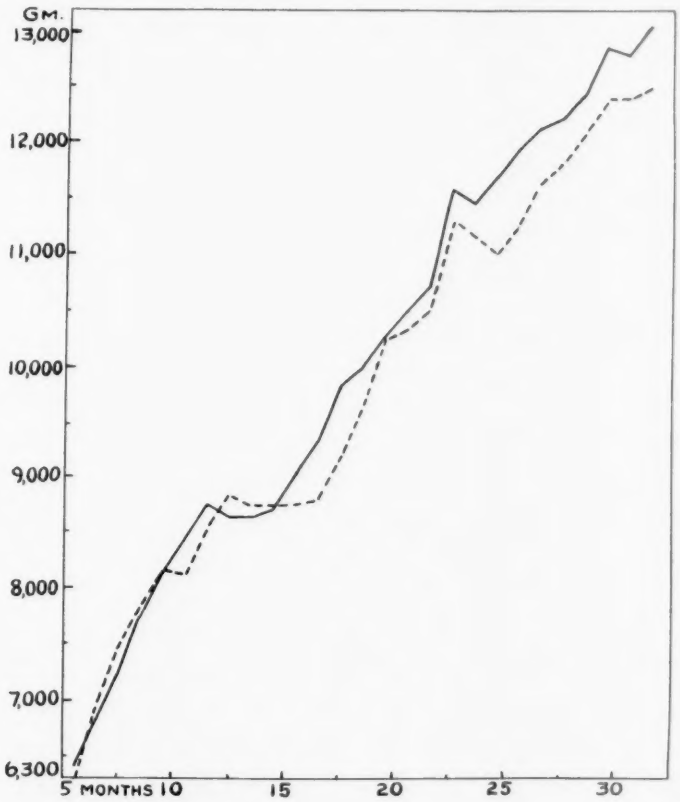

Fig. 1.—A composite curve showing the average weight of children of the same age plotted at two week intervals from the sixth to the thirtieth month. In this and the succeeding charts the solid line represents the curve for the group of 70 children given the special cereal mixture and the broken line, the corresponding curve for the control group of 66 children.

weights of children at the same age plotted at two week intervals from the age of 6 to 30 months.

At the beginning of the study the average weights for each group were practically identical. From the sixth to the fourteenth month the weight curve for the group given the special cereal was slightly below

that of the control group. At 14 months the average weight curve for the special group rose above that of the control group and remained higher throughout the period of observation. From the twelfth to the sixteenth month there was a leveling of both weight curves. This was thought to be due to decreased intake of food during the period of rapid eruption of the temporary teeth. We were unable to explain the peaks which occurred in both curves at the twenty-second and again

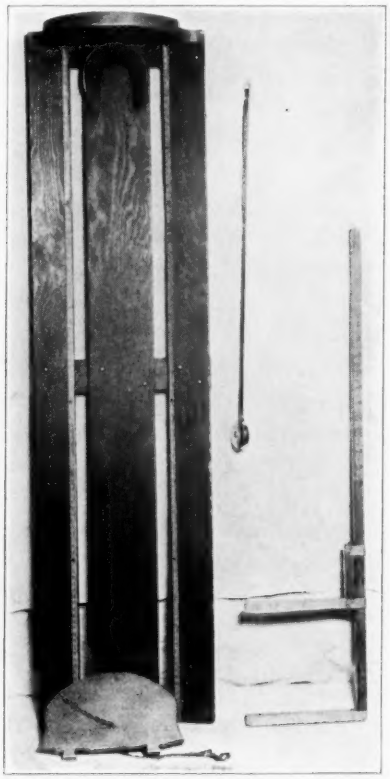

Fig. 2.—The board used in measuring the height of the children.

at the thirtieth month. In comparing our average weight curves with those taken from the Baldwin-Wood tables [7] we found that up to the eighteenth to twentieth month they coincided. Beyond the twentieth month, our curves rose above those of Baldwin and Wood.

Height.—The measuring board used to obtain the length of the children was a modification of the one described by Thompson [8] (figs.

7. Baldwin, B. T.: The Physical Growth of Children from Birth to Maturity, University of Iowa Studies in Child Welfare, 1920, vol. 1, no. 1.

8. Thompson, H.: A Measuring Board for Infants, Am. J. Phys. Anthrop. **13**:281 (July-Sept.) 1929.

1 and 2). An assistant held the head of the baby in position against the upper end of the board. The movable lower end was then brought against the soles of the feet with the legs forcibly extended. The reading was taken from the calibrations on either side of the board. The readings for height were grouped according to ages at the semi-monthly reading and were averaged. Figure 3 is a composite of the average readings for height taken at two week intervals from the sixth to the thirtieth month. It will be seen that up to the eighteenth month the curve for the special group coincided with or fell somewhat below that for the control group. At the eighteenth month the curve for

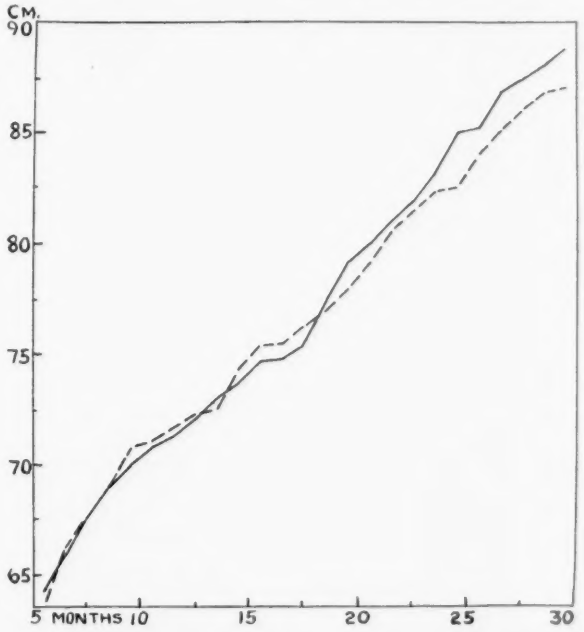

Fig. 3.—A composite curve showing the average height of children of the same age plotted at two week intervals from the sixth to the thirtieth month.

the special group rose above that for the control group, and it maintained this advantage for the remainder of the period of observation. These averages follow closely those of the Baldwin-Wood tables.

Sitting Height.—The sitting height or stem length, which is the distance from the vertex to the tuberosity of the ischium, was measured with the child in a reclining position on the measuring board. The average curves of stem length for the special and for the control groups (fig. 4) coincide closely with the height curves. In both instances the children receiving the special cereal mixture surpassed those receiving the usual cereal at about the sixteenth month.

Circumference of the Chest.—In the periodic examinations of these children, we noticed that there was a relation between the nutritional state of the child and the circumference of the chest. When there was a loss of weight due to vomiting, diarrhea or infection the circumference of the chest was reduced from a few millimeters to 2 cm., depending on the extent of the loss of weight. The subcutaneous fat over the ribs appeared to be utilized early whenever the reserve supply of fat was drawn on to maintain body metabolism. This observation was in accord with that of the Bakwins,[9] who found that the circumference of the

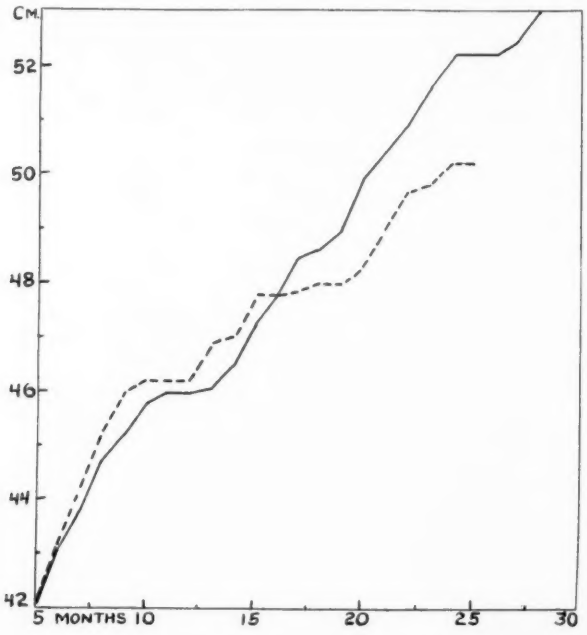

Fig. 4.—A composite curve showing the average sitting height or stem length of children of the same age plotted at two week intervals from the sixth to the thirtieth month.

thorax in a group of children suffering from acute intestinal indigestion fell below the average measurements for healthy infants.

In recording readings on the circumference of the chest Veracek [10] pointed out the importance of specifying axillary, mammary or xiphoid circumference. He called attention to the variation in the circumference of the chest taken on inspiration, expiration or between phases. Veracek showed that there is a variation in the circumference of the chest with

9. Bakwin, H., and Bakwin, R. M.: J. Clin. Investigation **10**:369, 1931.

10. Veracek, L.: Contribution à l'étude anthropométrique du périmètre thoyacique, Rev. anthropol. **41**:220 (July-Sept.) 1931.

the arms at the sides, crossed or raised. In our measurements the thoracic perimeter was taken at the mammary line during the respiratory phase midway between inspiration and expiration. The child's arms were free at the sides, and an average of three readings were recorded. The readings were again grouped according to age, and the average for each two week interval was used for the curves in figure 5. The curve for the special group was slightly below that for the control group until the eighteenth month, when the curve for the special group rose above that of the control group and maintained this position.

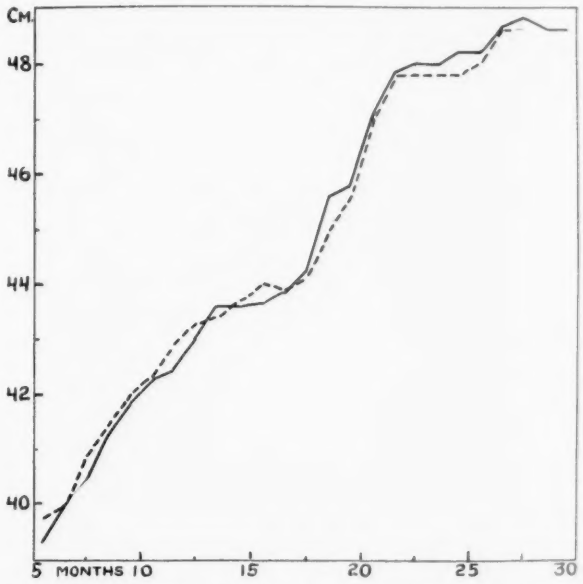

Fig. 5.—A composite curve showing the circumference of the chest of children of the same age plotted at two week intervals from the sixth to the thirtieth month.

Circumference of the Head.—This measurement was taken to observe whether the circumference of the head has any relation to the general nutritional state. We observed that only in those children in whom there was a loss of 6 ounces (170 Gm.) or more was there any decrease in circumference of the head. There were no children with abnormalities of the head due to syphilis, rickets, hydrocephalus or microcephalus in our groups (fig. 6). The curves of the averages for both groups ran almost parallel. A steel tape was used to measure the circumference of the chest and head.

Bicrestal Diameter.—This measurement, taken at the widest point of the iliac crests, was obtained with the sliding calipers shown in figure 2.

From it, according to Lucas and Pryor,[11] the type of body build may be determined. Their width-length index is $\frac{\text{bicrestal diameter} \times 100}{\text{height}}$. They found that a slender child with small bones has a low index while a broad child with large bones has a high index. According to their observations the general tendency is for this index to be higher for babies than for children because of the shortness of the bodies of the former. Using this index, the similarity of the children of our two groups was demonstrated (fig. 7). The index of the age groups in both the special and the control groups remained practically constant and similar, varying only between 16 and 16.5.

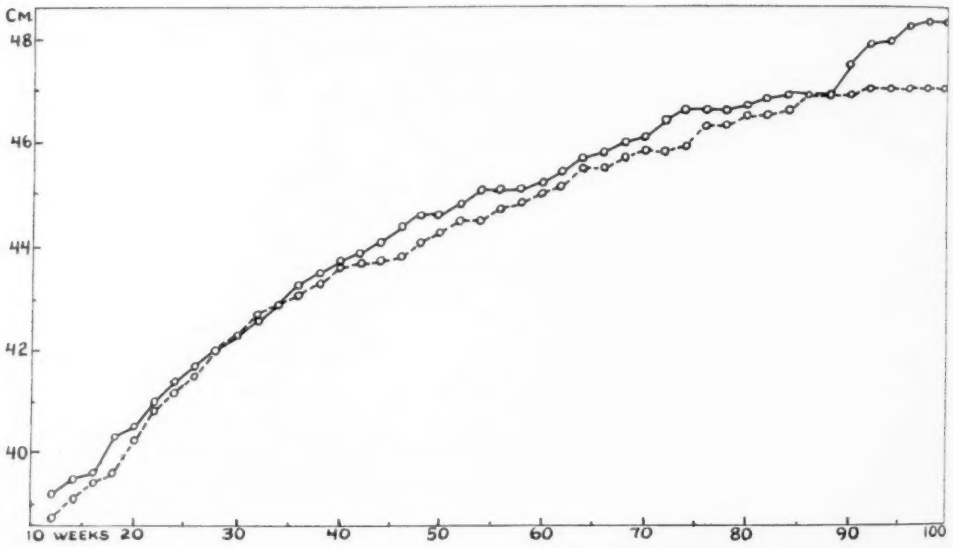

Fig. 6.—A composite curve showing the average circumference of the head of children of the same age plotted at two week intervals from the sixth to the thirtieth month.

Constitutional Index.—Of the numerous indexes for growth and development mentioned in standard texts on anthropometry we selected one which is based on measurements generally used in pediatric practice. Wilder[12] has expressed the opinion that the constitutional index is of value in determining the general health and resistance to disease of adults in the same racial group. For the constitutional index he used the fol-

11. Lucas, W. P., and Pryor, H. B.: Physical Measurements and Physiologic Processes in Young Children, J. A. M. A. **97**:1127 (Oct. 17) 1931; Growth Problems and Their Relation to Zones of Normal Physiologic Reactions, J. Pediat. **1**:572 (Nov.) 1932.

12. Wilder, H. H.: A Laboratory Manual of Anthropometry, Philadelphia, P. Blakiston's Son & Co., 1920.

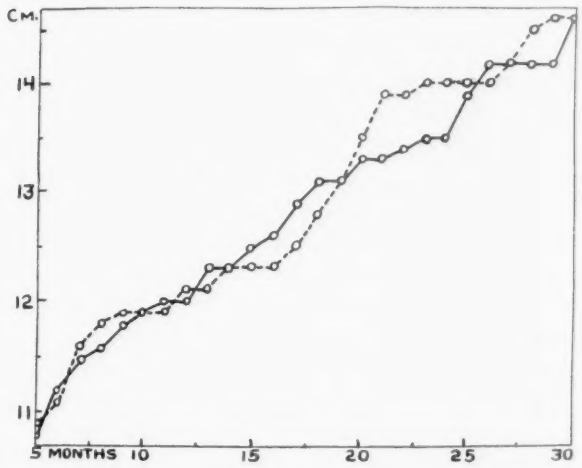

Fig. 7.—A composite curve showing the bicrestal diameter of children of the same age plotted at two week intervals from the sixth to the thirtieth month.

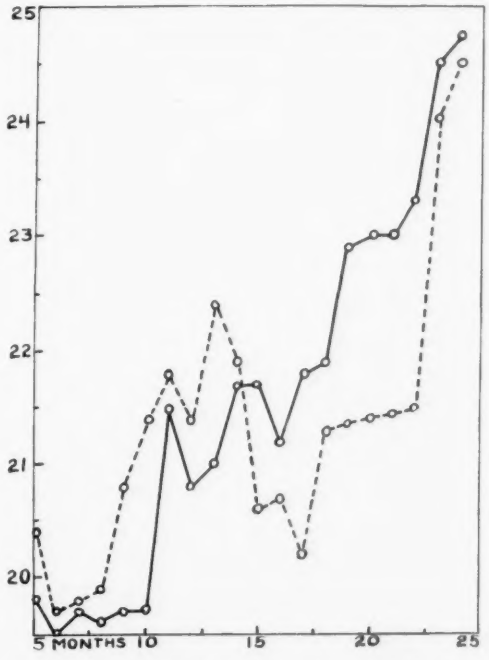

Fig. 8.—A composite curve showing the constitutional index of children of the same age plotted at two week intervals from the sixth to the thirtieth month.

lowing formula: height in centimeters minus (weight in kilograms plus maximum thoracic girth in centimeters). He stated that an index of 10 denotes a very strong constitution, from 16 to 20 good, from 21 to 25 fair, from 26 to 30 weak, and above 36 very weak.

To determine whether such an index has any relationship to the constitution of a group of infants and children or any of the individuals in the group we calculated the index for each child at each examination (fig. 8). The constitutional index for the age groups rose with an increase in age. At 5 months the average was 19 and at 30 months, 25. There was no apparent relationship between the incidence or seriousness of infection and the constitutional index in our group. An analysis of the indexes shows that with increasing age height increases more rapidly than weight plus circumference of the chest. This corresponds with the findings of Lucas and Pryor in their determination of the width-length index mentioned previously.

Figure 8 shows a drop in the index in both groups between the fifteenth and the eighteenth month, after which the index for the special group rose more rapidly than that for the control group. This can be explained by the more rapid increase in height which took place in the special group. The drop in both curves at the fifteenth to the eighteenth month was apparently due to a more rapid increase in the circumference of the chest in relationship to length in both groups during this interval.

Dentition.—On each examination the eruption of teeth was observed and tabulated. The age of eruption of the deciduous teeth was observed in 60 children in the special cereal group and in 52 in the control group.

Number of teeth	2	4	6	8	10	12	14	16	18	20
Average age of eruption by months	7.1	10.8	11.0	13.8	14.5	17.7	19.5	20.5	24.0	26.7
Control Group										
Average age of eruption by months	8.2	10.5	12.5	13.2	16.1	17.1	19.8	22.5	25.0	28.3

The tabulation shows that children in the special group had two teeth at the average age of 7.1 months while those in the control group were 8.2 months of age before two teeth had erupted. The children in the special group had twenty teeth at the age of 26.7 months, while those in the control group did not reach this point in development until the age of 28.3 months.

Incidence of Infection.—During the course of this study a number of the children had an infection of one kind or another. Infections of the upper respiratory tract predominated, with otitis media and bronchopneumonia following in the order of frequency. In our group of 126 children all were tested by either the Mantoux or the Pirquet method, and none gave a positive reaction to tuberculin or gave other evidence of tuberculous infection. There were no deaths in either group. In tabulating the incidence of infection in so small a group it was found impracticable to subdivide the groups further according to localization of infection. Those children who had mild symptoms in the upper

respiratory tract unaccompanied by a rise in temperature were not considered ill. The majority of the children went through the year of observation without illness accompanied by a temperature of 101 F. or over. All had rhinitis when "colds" were prevalent in the wards. This record of infection includes only those children whose rectal temperature reaches 101 F. or more. The duration of severity of

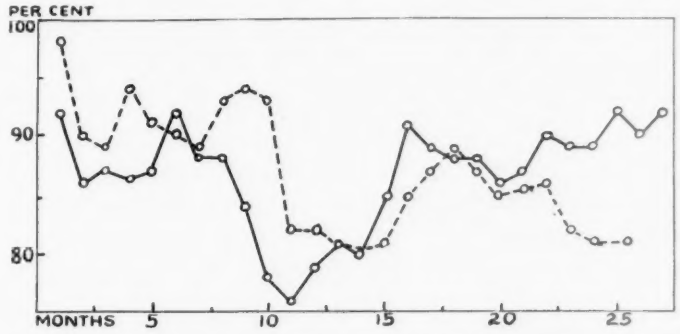

Fig. 9.—A composite curve showing the hemoglobin content, estimated according to Sahli's method, of children of the same age plotted at two week intervals from the sixth to the thirtieth month.

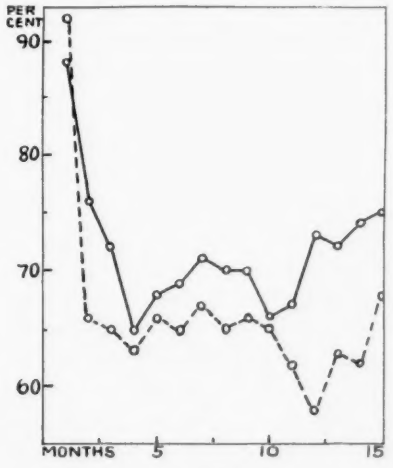

Fig. 10.—A composite curve showing the hemoglobin content, estimated according to Fleischl's method, of children of the same age plotted at two week intervals from the sixth to the thirtieth month.

infection was not considered—merely the incidence in each group. In the 70 children in the special group the incidence of infection accompanied by a temperature of 101 F. or more averaged 1.35 per individual for the year in comparison with the incidence in the control of 60 children of 2.18 per individual.

Hemoglobin.—Readings for hemoglobin were taken approximately once a month. Two types of hemoglobinometer were used, and readings were made by different persons. One used the Sahli hemoglobinometer and the other the Fleischl instrument exclusively. Results were grouped according to the scale used, as shown in figures 9 and 10. The results obtained on both scales show the average hemoglobin reading after the fifteenth month to be higher for the special group than for the control group. The readings taken with the Sahli scale (fig. 9) were uniformly higher than those taken with the Fleischl scale (fig. 10).

Results.—Roentgen examination of the wrists of both groups of children made early in the study and at its termination showed no evidence of active rickets. Antirachitic prophylaxis is used as a routine for all children at the institution. Evidence of mild healed rickets was observed in a few cases.

CONCLUSIONS

Graphs show that the group fed the special cereal mixture exceeded the control group in weight, total length, stem length and circumference of the chest and head. From the records of dentition it is seen that those fed the special cereal mixture had an earlier eruption of teeth. Hemoglobin curves show an advantage in favor of the group receiving the special cereal. No relationship was observed between the constitutional index and the incidence of infection. Figures for the constitutional index rise with advancing age. Wilder's method of application of the constitutional index to adult racial groups was not applicable to our group of infants.

SUMMARY

A group of children at St. Vincent's Infant and Maternity Hospital was divided into two sections. One section was fed as the cereal dietary component a special mixture devised by Tisdall, Drake and Brown, while the second was given the usual cereals. The two groups were as nearly equal in age, sex, race, social status, body build and management as selection from children in one institution would allow. All received the usual diet for their respective ages, and no cereal was forced. A record of weight, height, stem length, circumference of head and chest and bicrestal diameter was made at two week intervals for a twelve month period. Determinations on hemoglobin content and observations on dentition and incidence of infection were made at each examination. From measurements obtained, the constitutional index was computed. No child refused cereal of any type, nor were there any allergic manifestations that could be attributed to its use.

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PRENATAL CONDITIONS AND THE STATUS OF INFANTS AT BIRTH

OBSERVATIONS

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This study was undertaken with the hope of clarifying the relationship between certain maternal conditions during pregnancy and the state of well-being of the fetus at birth, as measured by length, weight, development of bone and blood calcium.

Present researches in the field of human prenatal development continue to show how difficult it is to demonstrate cause and effect in growth, since it is virtually impossible to secure subjects who live under sufficiently similar conditions to have truly common factors as a basis for comparison. Although this study is based on a group of subjects who had few significant factors in common, the facts are presented because the group was large and the conditions under which the observations were made were unusually uniform and favorable for a fairly accurate analysis and sorting of data.

METHOD OF INVESTIGATION

This study was made in Dayton, Ohio, on a group of about two hundred women, charity patients in the infant and maternity clinic of the Miami Valley Hospital. They appeared for observation antepartum in order to secure medical attention at delivery at minimum cost and not primarily for the treatment of abnormal physical conditions. The observations on prenatal and postnatal environment of the child were made by a Fels Fund worker, who had ready access both to the subjects and to their homes through the intelligent and efficient cooperation of the Visiting Nurses' Association of Dayton. The dietary histories were obtained by a medical attendant during the mother's stay in the hospital. Diet sheets contained a comprehensive list of foods with space after each food in which was recorded the mother's statement of how frequently and in what quantities the food had been eaten. Space was also provided for unlisted foods. Within three months following the taking of this history, a field worker went into the home of the subject and took a new record in a similar manner. If the two histories differed materially, they were discarded. The diet sheets were then evaluated by a dietitian and a pediatrician. A four category qualitative rating scale was devised to show the adequacy of each subject's diet in the various chemical elements for

From the Samuel S. Fels Fund at Antioch College.

which it could be evaluated. The roentgenograms of the infants were taken at the hospital as soon after birth as the condition of the child permitted. The total epiphyseal area was measured at the laboratory of the Fels Fund by the Coradi disk planimeter. Measurements of the infants and determinations of the serum calcium of the blood of the mother at delivery and of the serum calcium of the cord blood were made at the hospital by the method employed as a routine.

Subjects were excluded whose medical charts showed evidence of marked pathologic lesions or of physical conditions existing during pregnancy which are known to interfere with prenatal development. Premature infants and those whose weights exceeded the mean weight at birth for infants in Iowa (boys, 8.32 ± 0.04 pounds [$3{,}773.9 \pm 18.1$ Gm.]; girls, 7.68 ± 0.04 pounds [$3{,}483.6 \pm 18.1$ Gm.]) [1] by plus or minus four times the probable error of the mean were also excluded. One hundred and two boys and eighty-seven girls were used in the study.

The data on the living conditions were secured by visits to the homes by two trained social workers, who evaluated the conditions of the home from its general size and appearance, the number of people living together and the means of support, income, property ownership and kind of jobs held by the infant's parents just before the birth of the child. The home environment was then rated as "very good," "good," "fair," "poor" and "wretched."

DIFFERENCES BASED ON SEX

Length and Weight.—The boys ranged in length from 45.5 to 53.4 cm. with an average length of from 49.5 to 50 cm., and the girls from 46 to 55 cm. with an average length of approximately 50 cm. These values revealed no significant difference based on sex.

The boys ranged in weight from 4.69 to 9.83 pounds (2,127.35 to 4,458.81 Gm.), with an average of 7.44 ± 0.08 pounds ($3{,}374.72 \pm 36.29$ Gm.). The girls ranged in weight from 5.52 to 10.12 pounds (2,503.83 to 4,590.35 Gm.), with an average of 7.24 ± 0.09 pounds ($3{,}284.01 \pm 40.82$ Gm.). The standard deviations were, respectively, 1.28 and 1.06 pounds (580.60 and 480.81 Gm.). The difference between the sexes is not significant.

Calcium of the Blood of the Cord.—The average calcium content of the blood of the cord for the boys was 9.51 ± 0.10 mg. per hundred cubic centimeters, with a coefficient of variability of 11.78 ± 0.75. The range was from 7.30 to 12.10 mg. The average calcium content for the girls was 9.38 ± 0.14 mg. with a range of from 7.26 to 12.10 mg. The ratio between the two means was 1.31, indicating a difference according to sex of doubtful significance.

Length and Maturity of Bones.—Most investigators have demonstrated a difference between the sexes in the development and maturity of bone at various age levels. In this group the difference between the sexes was not pronounced when the total epiphyseal area and length of the bones were considered. When the number of epiphyses having

1. Iowa Child Welfare Research Station, State University of Iowa: Physical Traits of Iowa Infants, Am. J. Dis. Child. **42**:1137 (Nov.) 1931.

nuclei of calcification and tarsal and carpal nuclei is also considered, a difference between the sexes was still not convincingly evident. Neither was the variability greater in one sex than in the other (the coefficient of variability for the boys being 67.24 ± 4.38 and for the girls, 67.69 ± 5.00). Since other studies have shown that boys usually weigh more at birth than girls, this lack of difference between the sexes

Product-Moment Correlations Between Various Fetal and Maternal Factors

Sex Group	Traits Correlated	Number of Subjects	Product-Moment Correlations	Probable Error of the Correlations
M	Length and weight	42	+0.46	±0.08
F	Length and weight	25	+0.27	±0.13
M	Weight and total epiphyseal area	102	+0.44	±0.05
F	Weight and total epiphyseal area	80	+0.50	±0.06
M and F	Caloric intake of mother and weight at birth	92	−0.06	±0.07
M	Serum calcium of mother and child	56	+0.85	±0.02
F	Serum calcium of mother and child	35	+0.90	±0.02
M and F	Maternal serum calcium and total epiphyseal area	76	+0.10	±0.08
M	Length at birth and total epiphyseal area	42	+0.31	±0.09
M and F	Total adequacy of mother's diet and epiphyseal area	88	+0.06	±0.07
M and F	Length of femur and epiphyseal area	50	+0.48	±0.07
M and F	Total adequacy of mother's diet and length of femur	81	+0.15	±0.07
M and F	Calcium in diet of mother and serum calcium of the cord blood	53	−0.13	±0.09
M and F	Mother's gain in weight and weight at birth	27	−0.11	±0.11
M and F	Mother's caloric intake and area of ossification	54	+0.07	±0.09
M	Mother's intake of protein and total epiphyseal area	48	−0.06	±0.09
M	Carbohydrate in mother's diet and total epiphyseal area	48	−0.12	±0.09
M	Fat in mother's diet and total epiphyseal area	49	+0.01	±0.09
M and F	Calcium in mother's diet and total epiphyseal area	69	+0.11	±0.08
M and F	Phosphorus in mother's diet and total epiphyseal area	68	+0.23	±0.08
M and F	Prenatal age and total epiphyseal area	76	+0.21	±0.07
M and F	Mother's diet and conditions in the home	62	+0.01	±0.06

may be wholly due to the sampling. The girls in this series were nearly as large as the boys and might have been expected to be more mature skeletally than girls usually are at birth.

RELATIONSHIP BETWEEN MATERNAL AND FETAL FACTORS

The data included in the table are self-explanatory; the product-moment correlation values were obtained by comparison of the factors which could be derived from the data. Means were calculated for the

traits in which it seemed that differences based on sex might appear. However, since the principal object of the study was to test the relationship existing between factors rather than to establish norms, boys and girls were grouped together unless the number in either sex group was large enough to make a satisfactory sampling. In that case the traits for one sex only were compared, in order to rule out the effects of possible differences based on sex.

The data included in the table give little evidence (within the limits determined in this study and those of the accuracy of the histories) of relationship between nutrition and the weight at birth, the length at birth or the degree of skeletal growth at birth. There is no conclusive evidence in the literature that there is or is not such a relationship.

Toverud,[1a] in an analysis of statistics gathered in Norway, found a significant increase in the weight of infants born during August and October. In discussing the possible causes of this difference in weight, she mentioned the increase in sunlight during the summer months, the increased availability of fresh fruits and vegetables and the greater amount of time which the mothers probably spent at rest during the warm months. She was inclined to attribute the seasonal differences in weight in her series to a combination of these factors. Abels [2] found a similar increase in the weight at birth during the summer months.

The results of our study suggest that sunshine and rest may have been more important factors than the caloric intake in the increase of weight in Toverud's and Abels' [2] series. Gerschenson [3] attributed such seasonal variations in weight to differences in the amount of sunlight. In a series of subjects studied at the Institute for Mother and Child Welfare at Odessa, U. S. S. R., he also reported a large increase in the number of infants of light weight (under 2,500 Gm.) who were born during the famine years of 1921 and 1922. In the study presented here, however, in no instance did the caloric intake even approach that which would be common during a famine. We should not, therefore, expect our evidence to test that of Gerschenson. Adair and Thelander [4] and de Aberle [5] and her co-workers found that there was a relationship

1a. Toverud, K. U.: Nutritional Condition of New-Born Infants: A Statistical Study, Am. J. Dis. Child. **46**:954 (Nov.) 1933.

2. Abels, H.: Klin. Wchnschr. **1**:1785, 1922.

3. Gerschenson, A. O.: The Influence of Several Factors on the Weight of the Newborn Infant, Ztschr. f. Kinderh. **51**:20, 1931.

4. Adair, F. L., and Thelander, H.: Weight and Dimensions of Human Placenta in Its Relation to Weight of Newborn Infant, Am. J. Obst. & Gynec. **10**:172, 1925.

5. de Aberle, S. B.; Morse, A. H.; Thompson, W. R., and Pitney, E. H.: The Relation of the Weight of the Placenta, Cord and Membranes to the Weight of the Infant in Normal Full-Term and in Premature Deliveries, Am. J. Obst. & Gynec. **20**:397, 1930.

between the size of the placenta and the weight at birth. That there is no common agreement concerning the effect of a high amount of sugar in the maternal blood on the weight at birth adds strength to the argument against a definite correlation between the weight at birth and the maternal caloric intake.

The literature is as barren of conclusive evidence of the significance of the intake of calcium and phosphorus in determining the size of the centers of ossification at birth as it is regarding the relation of the weight at birth to the caloric intake. From what is known regarding the seeming independence of the growth of new bone (or at least the transformation of cartilage into osteoid tissue) and rickets, it seems probable that the intake of calcium, phosphorus and vitamin D is more important in the determination of the density of bone than in its growth. It is therefore not difficult to understand the existence of a low value for the correlation between calcium and phosphorus in the maternal diet and the area of ossification at birth. It is unfortunate that a satisfactory and accurate method of comparing the densities of bone in this series was not available.

The correlation which was made between the mother's diet and the home conditions means little, but the values are included to help in showing quantitatively what the facts were. Even the "best homes" were somewhat meager, since all the families represented a class in need of financial help. Because the data were collected during the years 1931 and 1932, during the depression, many families which previously had been able to maintain fairly good homes were dependent on the local relief organizations for food, although the household furnishings, acquired during better times, belied the fact.

CONCLUSIONS

The material for the part of the study which dealt with maternal nutrition was collected in a manner more or less universally used by physicians and nutrition workers. The records probably were obtained as carefully as were most of the data on allied subjects available in the literature. They were evaluated independently by two nutrition workers, the evaluations were checked, and differences discussed. The correlations which deal with such quantitatively measurable factors as length, weight, blood calcium and development of bone should be significant. The lack of evidence of a relationship existing between various prenatal nutritional factors and fetal growth might be considered as evidence that no such relationship exists. This may be the true situation. We believe, however, that while this work has added something to the available information on the subject, to us it has also pointed out the necessity and economy, in the final analysis, of concentrating our efforts on a quantitative study of the relations existing between

prenatal nutrition and fetal growth. Such a study is difficult, tedious and expensive. It necessitates the use of a weighed diet from which aliquots are regularly taken for quantitative chemical analysis of all the important nutritive elements. The weighing and recording are so burdensome to most patients that they are unwilling to undertake the task. The number of analyses of foodstuffs and excreta is so great that a considerable staff of analysts is required to handle them, even for two or three subjects at a time. There are many details, such as daily activity, emotional changes, etc., which must be watched. Despite all these difficulties, the quantitative method seems to us the most desirable, if not the only, method by which decisive information can be obtained.

SUMMARY

1. A group of one hundred and two boys and eighty-seven girls were used in this study.

2. The difference in weight between the sexes was of questionable significance.

3. No significant difference between the sexes in length or in the serum calcium content of the blood of the cord was noted.

4. A positive correlation was shown between the calcium content of the blood of the mother and that of the cord, the weight at birth and the epiphyseal area and between the length of the femur and the epiphyseal area.

5. A positive correlation was shown between the length at birth and the weight at birth for boys but not for girls.

6. No correlation was shown between the following sets of factors: (*a*) the calcium content of the serum of the mother and the total fetal epiphyseal area; (*b*) the length at birth and the fetal epiphyseal area; (*c*) the adequacy of the maternal diet and the fetal epiphyseal area; (*d*) the adequacy of the maternal diet and the length of the femur; (*e*) the amount of calcium in the maternal diet and the calcium content of the serum of the cord; (*f*) the mother's gain in weight and the weight at birth; (*g*) the mother's caloric intake and the weight at birth; (*h*) the mother's intake of protein and the fetal epiphyseal area; (*i*) the amount of carbohydrate in the mother's diet and the fetal epiphyseal area; (*j*) the amount of fat in the mother's diet and the fetal epiphyseal area; (*k*) the amount of calcium in the mother's diet and the fetal epiphyseal area; (*l*) the amount of phosphorus in the mother's diet and the fetal epiphyseal area; (*m*) the menstrual age of the fetus and the fetal epiphyseal area; (*n*) the diet of the mother and the home conditions.

ERYTHROCYTE, HEMOGLOBIN, CELL VOLUME AND COLOR, VOLUME AND SATURATION INDEX STANDARDS FOR NORMAL CHILDREN OF SCHOOL AGE

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So few are the reliable observations of the hemoglobin content of the blood during infancy and childhood that it would seem unwise to make a more precise statement concerning the average values and the normal limits of variation for the different age groups. . . . The data concerning red cell counts during infancy and childhood are so meager and so conflicting that no final statements can be made concerning the average values for the age periods nor the normal limits of variation. . . . The important values are not the averages, but the average limits of variation. It is just these which are particularly uncertain.

This quotation from the report of the White House Conference on Child Health and Nutrition [1] indicates clearly the need for the study of normal hematologic standards in children. To help fill this need we have determined the red cell count, hemoglobin content and erythrocyte volume and have calculated the hemoglobin and volume coefficients and the color, volume and saturation indexes of 215 healthy children ranging in age from 4 to 13 years, inclusive, about equally distributed as to age and sex.

All the children lived in or near Portland, at an elevation of less than 500 feet. All were white and native-born—in most instances being children of native-born parents. They were from the public grade schools, orphanages and baby homes, physicians' families and the outpatient clinic. Those from the outpatient clinic had been brought in for tonsillectomy but were found by the examining physician to have no indications for this operation. The results from children in different social classes were at first averaged separately, but no significant dif-

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1. White House Conference on Child Health and Protection: Growth and Development of the Child: Part 2. Anatomy and Physiology, New York, D. Appleton-Century Company, 1932, p. 365.

ferences were found. All the children had had a recent physical examination and stated at the time the blood was taken that they felt well. It seems justifiable to regard these subjects as representative of the healthy white children of the Pacific northwest.

METHODS

Since the methods used have been described in detail elsewhere,[2] they will be commented on only briefly here. Venous blood mixed with 2 mg. of dry potassium oxalate per cubic centimenter was used for all determinations and is recommended for routine use because of the convenience and greater accuracy of the results. No difficulty was encountered in obtaining blood from the vein, even in the younger children. The blood was taken at any time of day, as in the course of ordinary office practice.

The red cell count was made with apparatus certified by the Bureau of Standards, using Toisson's diluting fluid. Two or more counts on separate dilutions agreeing within 100,000 cells per cubic millimeter were averaged.

The estimations of hemoglobin were done with care by the Osgood-Haskins[2] hemoglobin method[3] which, although a simple clinical method, has been shown[4] to give results comparable in accuracy to the Van Slyke oxygen capacity method or the blood iron method. The results are expressed both in grams per hundred cubic centimeters and in percentage, 100 per cent by this method equaling 13.8 Gm. per hundred cubic centimeters.

The cell volume[5] was determined by centrifugation to constant volume in the Osgood-Haskins cell volume tube.[6] A correction for shrinkage caused by the oxalate by the addition of 3.5 per cent of the volume of packed cells should be made if one wishes to compare the results with isotonic anticoagulants.

Hemoglobin coefficient was suggested (E. E. O.) as a term for the grams of hemoglobin which 100 cc. of blood would contain if the red cell count were 5,000,000 per cubic millimeter. It is calculated by the proportion: red cell count:

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2. (*a*) Osgood, E. E.; Haskins, H. D.; Trotman, F. E., and Mathieu, A.: A Uniform System of Hematologic Methods for Use with Oxalated Venous Blood: A Simplification of the Osgood-Haskins Hemoglobin Method; a Rapid Method for Determination of the Sedimentation Rate of the Red Cells with Results in Health and Disease, J. Lab. & Clin. Med. **16**:476 (Feb.) 1931. (*b*) Osgood, E. E., and Haskins, H. D.: Relation Between Cell Count, Cell Volume and Hemoglobin Content of Venous Blood of Normal Young Women, Arch. Int. Med. **39**:643 (May) 1927. (*c*) Osgood, E. E.: A Textbook of Laboratory Diagnosis, ed. 2, Philadelphia, P. Blakiston's Son & Company, 1935, pp. 178 and 392; Hemoglobin, Color Index, Saturation Index and Volume Index Standards, Arch. Int. Med. **37**: 685 (May) 1926.

3. The standard is obtainable from Hynson, Westcott and Dunning, Baltimore.

4. Dowden, C. W.; McNeill, C., and McNeill, J. D.: A Clinical Study of Blood Iron and Hemoglobin, J. Lab. & Clin. Med. **19**:362 (Jan.) 1934.

5. Osgood and Haskins.[2b] Osgood.[2c]

6. This instrument is obtainable from the Arthur H. Thomas Company, Philadelphia.

5,000,000 : : hemoglobin : x. The corpuscular hemoglobin of Wintrobe [7] is estimated as the average hemoglobin content of one red cell in micromicrograms and may be determined by multiplying the hemoglobin coefficient by 2.[8]

The volume coefficient is similarly an expression for the volume of packed cells which 100 cc. of blood would contain if the red cell count were 5,000,000 per cubic millimeter. It is calculated by the proportion: red cell count : 5 : : cell volume : x. The corpuscular volume of Wintrobe [7] may be determined by multiplying the volume coefficient by 2, giving the average volume of one red cell in cubic microns.

TABLE 1.—*Results of Studies of the Blood of Boys and Girls 4 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	5.74	77.6	10.71	9.35	0.78	34.43	30.05	0.83	0.93
	5.61	85.7	11.83	10.54	0.88	37.23	33.23	0.92	0.95
	5.04	94.2	13.00	12.89	1.07	38.87	38.56	1.07	1.00
	5.15	87.8	12.12	11.76	0.98	35.28	34.25	0.95	1.03
	4.70	83.0	11.45	12.19	1.02	34.16	36.34	1.01	1.01
	4.54	87.3	12.05	13.27	1.11	34.06	37.51	1.04	1.06
	4.30	68.2	9.41	10.94	0.91	28.88	33.59	0.93	0.98
	4.42	73.1	10.09	11.41	0.95	30.59	34.61	0.96	0.99
	4.80	72.9	10.06	10.48	0.87	28.76	29.96	0.83	1.05
	4.46	71.2	9.83	11.02	0.92	34.06	38.18	1.06	0.87
	4.11	87.1	12.02	14.62	1.22	30.86	37.55	1.04	1.17
Average	4.81	80.7	11.14	11.68	0.97	33.38	34.89	0.97	1.00
Maximum	5.74	94.2	13.00	14.62	1.22	38.87	38.56	1.07	1.17
Minimum	4.11	68.2	9.41	9.35	0.78	28.76	29.96	0.83	0.87
				Girls					
	4.44	75.8	10.46	11.78	0.98	33.33	37.54	1.04	0.94
	5.58	87.8	12.12	10.86	0.91	34.37	30.80	0.86	1.06
	5.48	91.3	12.60	11.50	0.96	36.99	33.75	0.94	1.02
	5.08	88.6	12.23	12.03	1.00	36.65	36.07	1.00	1.00
	4.87	86.1	11.88	12.20	1.02	35.99	36.95	1.03	0.99
	4.48	80.9	11.05	12.34	1.03	35.29	39.39	1.09	0.94
	4.41	82.2	11.34	12.86	1.07	33.22	37.66	1.05	1.02
	5.59	99.4	13.72	12.27	1.02	37.50	33.54	0.93	1.10
	5.04	103.6	14.30	14.18	1.18	36.65	36.36	1.01	1.17
	4.66	89.8	12.39	13.29	1.11	31.25	33.50	0.93	1.19
Average	4.96	88.5	12.21	12.33	1.03	35.12	35.56	0.99	1.04
Maximum	5.59	103.6	14.30	14.18	1.18	37.50	39.39	1.09	1.19
Minimum	4.41	75.8	10.46	10.86	0.91	31.25	30.80	0.86	0.94
				Boys and Girls					
Average	4.85	84.5	11.65	11.99	1.00	34.21	35.21	0.98	1.02
Maximum	5.74	103.6	14.30	14.62	1.22	38.87	39.39	1.09	1.19
Minimum	4.11	68.2	9.40	9.35	0.78	28.76	29.96	0.83	0.87

The color index is:

$$\frac{\text{hemoglobin expressed as percentage of average normal hemoglobin coefficient}}{\text{red cell count expressed as percentage of 5,000,000}}$$

The volume index is:

$$\frac{\text{cell volume expressed as percentage of average normal coefficient}}{\text{red cell count expressed as percentage of 5,000,000}}$$

The saturation index is:

$$\frac{\text{hemoglobin expressed as percentage of average normal hemoglobin coefficient}}{\text{cell volume expressed as percentage of average normal volume coefficient}}$$

7. Wintrobe, M. M.: Size and Hemoglobin Content of the Erythrocyte, J. Lab. & Clin. Med. **17**:899 (June) 1932.

8. $$\frac{\text{1,000,000,000,000 micromicrograms per gram}}{\text{5,000,000 red blood cells per cu. mm.} \times \text{100,000 cu. mm. per 100 cc.}} = 2$$

Wintrobe's corpuscular hemoglobin concentration[7] may be calculated in percentage by dividing the number of grams of hemoglobin per hundred cubic centimeters by the number of cubic centimeters of packed red cells per hundred cubic centimeters and multiplying by 100. Since there were no significant variations

TABLE 2.—*Results of Studies of the Blood of Boys and Girls 5 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	4.88	71.8	9.91	10.15	0.85	32.76	33.57	0.93	0.91
	5.00	88.5	12.21	12.21	1.02	35.24	35.24	0.98	1.05
	5.37	83.0	11.45	10.66	0.89	34.17	31.82	0.88	1.01
	5.08	83.2	11.48	11.30	0.94	34.10	33.56	0.93	1.01
	4.62	91.1	12.57	13.61	1.13	37.33	40.40	1.12	1.01
	4.38	78.4	10.82	12.35	1.03	32.46	37.06	1.03	1.00
	4.76	86.0	11.87	12.47	1.04	35.48	37.27	1.04	1.00
	4.41	88.1	12.16	13.78	1.15	35.12	39.82	1.11	1.04
	5.20	84.3	11.63	11.19	0.93	34.64	33.31	0.93	1.01
	5.03	77.2	10.65	10.59	0.88	35.68	35.47	0.99	0.90
	5.38	92.5	12.77	11.86	0.99	36.47	33.90	0.94	1.05
Average	4.92	84.0	11.59	11.83	0.99	34.86	35.58	0.99	1.00
Maximum	5.38	92.5	12.77	13.78	1.15	37.33	40.40	1.12	1.05
Minimum	4.38	71.8	9.91	10.15	0.85	32.46	31.82	0.88	0.90
				Girls					
	5.11	74.2	10.24	10.02	0.83	33.00	32.29	0.90	0.93
	4.66	76.3	10.53	11.30	0.94	32.27	34.62	0.96	0.98
	4.98	85.3	11.77	11.82	0.99	35.98	36.13	1.00	0.98
	4.58	71.7	9.89	10.80	0.90	32.70	35.78	0.99	0.91
	4.98	82.2	11.34	11.39	0.95	35.11	35.26	0.98	0.97
	5.09	85.5	11.80	11.59	0.97	35.75	35.12	0.98	0.99
	4.90	80.6	11.12	11.35	0.95	33.79	34.48	0.96	0.99
	4.73	83.7	11.55	12.21	1.02	34.88	36.34	1.01	1.01
	5.23	84.4	11.65	11.13	0.93	32.98	31.53	0.88	1.06
	4.06	93.2	12.86	15.84	1.32	33.00	40.64	1.13	1.17
Average	4.83	81.7	11.28	11.75	0.98	33.90	35.22	0.98	1.00
Maximum	5.23	93.2	12.86	15.84	1.32	35.98	40.64	1.13	1.17
Minimum	4.06	71.7	9.89	10.02	0.83	32.27	31.53	0.88	0.91
				Boys and Girls					
Average	4.88	82.9	11.44	11.79	0.98	34.40	35.41	0.98	1.00
Maximum	5.38	83.2	12.86	15.84	1.32	37.33	40.64	1.13	1.17
Minimum	4.06	71.7	9.89	10.02	0.83	32.27	31.53	0.88	0.90

with age or sex in the hemoglobin coefficient or volume coefficient in the group under consideration the average values for the whole group were used in calculating the color, volume and saturation indexes. Tables greatly simplifying the calculation of the indexes have been devised.[9]

9. Osgood, E. E.: Tables for Calculation of Color Index, Volume Index and Saturation Index Based on Recently Determined Standards, J. Lab. & Clin. Med. **12**:899 (June) 1927; Tables for Calculation of Color Index, Volume Index and Saturation Index in Childhood and Adolescence, to be published. Osgood and Haskins.[2b] Osgood.[2c]

TABLE 3.—*Results of Studies of the Blood of Boys and Girls 6 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	5.07	79.5	10.97	10.82	0.90	34.30	33.83	0.94	0.96
	5.32	91.6	12.64	11.88	0.99	35.49	33.36	0.93	1.07
	4.98	88.9	12.27	12.54	1.05	34.81	34.95	0.97	1.08
	5.96	91.5	12.63	10.59	0.88	37.06	31.09	0.86	1.02
	5.14	78.3	10.81	10.51	0.88	34.65	33.71	0.94	0.94
	5.27	81.8	11.29	10.71	0.89	35.71	33.88	0.94	0.95
	4.19	83.8	11.56	13.80	1.15	32.69	39.01	1.08	1.06
	4.20	79.1	10.92	13.00	1.08	32.37	38.53	1.07	1.01
	4.85	82.6	11.40	11.75	0.98	34.38	35.45	0.98	0.99
Average	5.00	84.1	11.61	11.74	0.98	34.61	34.87	0.97	1.01
Maximum	5.96	91.6	12.64	13.80	1.15	37.66	39.01	1.08	1.08
Minimum	4.19	78.3	10.81	10.51	0.88	32.37	31.09	0.86	0.94
				Girls					
	5.08	95.4	13.16	12.96	1.08	36.93	36.35	1.01	1.07
	5.20	89.2	12.31	11.84	0.99	36.65	35.24	0.98	1.01
	4.40	75.8	10.46	11.89	0.99	32.39	36.81	1.02	0.97
	4.95	81.4	11.23	11.35	0.95	37.62	38.00	1.06	0.90
	4.68	80.5	11.11	11.87	0.99	31.55	33.71	0.94	1.06
	5.32	99.9	13.79	12.95	1.08	37.61	35.35	0.98	1.10
	5.50	85.9	11.85	10.78	0.90	35.05	31.87	0.89	1.01
	4.43	83.0	11.45	12.93	1.08	34.50	38.94	1.08	1.00
	4.90	81.6	11.26	11.49	0.96	35.87	36.60	1.02	0.94
	5.18	78.0	10.76	10.39	0.87	34.38	33.19	0.92	0.94
	5.07	85.0	11.73	11.57	0.96	37.47	36.95	1.03	0.94
	5.15	93.9	12.96	12.58	1.05	37.65	36.56	1.02	1.03
	4.36	80.5	11.11	12.74	1.06	33.66	38.60	1.07	0.99
Average	4.94	85.4	11.78	11.95	1.00	35.49	36.01	1.00	1.00
Maximum	5.50	99.9	13.79	12.96	1.08	37.65	38.94	1.08	1.07
Minimum	4.36	75.8	10.46	10.39	0.87	31.55	31.87	0.89	0.90
				Boys and Girls					
Average	4.97	84.9	11.71	11.86	0.99	35.13	35.54	0.99	1.00
Maximum	5.96	99.9	13.79	13.80	1.15	37.65	39.10	1.08	1.08
Minimum	4.19	75.8	10.46	10.39	0.87	31.55	31.09	0.86	0.90

TABLE 4.—*Results of Studies of the Blood of Boys and Girls 7 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	5.07	78.0	10.76	10.61	0.88	36.63	36.12	1.00	0.88
	5.16	87.5	12.07	11.70	0.97	36.12	35.00	0.97	1.00
	4.41	76.5	10.56	11.97	1.00	32.71	37.09	1.03	0.97
	5.35	87.0	12.01	11.22	0.94	39.19	36.63	1.02	0.92
	5.11	82.5	11.38	11.14	0.93	36.30	35.52	0.99	0.94
	4.81	80.1	11.05	11.49	0.96	34.57	35.94	1.00	0.96
	5.34	86.9	11.99	11.23	0.94	39.06	36.58	1.02	0.92
	4.74	83.6	11.54	12.17	1.01	33.86	35.71	0.99	1.02
	4.22	78.2	10.79	12.79	1.07	32.92	39.01	1.08	0.98
	4.88	81.6	11.26	11.54	0.96	33.98	34.81	0.97	0.99
	4.99	86.6	11.95	11.97	1.00	35.02	35.09	0.97	1.02
Average	4.92	82.6	11.40	11.62	0.97	35.49	36.14	1.00	0.96
Maximum	5.35	87.5	12.07	12.79	1.07	39.19	39.01	1.08	1.02
Minimum	4.22	76.5	10.56	10.61	0.88	32.71	34.81	0.97	0.88
				Girls					
	5.26	88.3	12.19	11.57	0.96	33.49	31.83	0.88	1.09
	5.36	87.0	12.01	11.25	0.94	35.60	33.21	0.92	1.02
	4.96	89.9	12.41	12.51	1.04	41.45	41.78	1.16	0.90
	4.46	91.9	12.68	14.22	1.18	34.78	38.99	1.08	1.09
	4.88	82.2	11.34	11.62	0.97	32.44	33.24	0.99	1.05
	5.07	91.9	12.68	12.51	1.04	36.21	35.71	0.99	1.05
	5.39	79.9	11.03	10.23	0.85	35.96	33.36	0.93	0.92
	5.68	93.7	12.93	11.38	0.95	40.96	36.06	1.00	0.95
	5.23	90.6	12.50	11.98	1.00	35.29	33.74	0.94	1.07
	4.14	80.0	11.04	13.33	1.11	34.22	41.32	1.15	0.97
Average	5.04	87.5	12.08	12.06	1.00	36.04	35.92	1.00	1.01
Maximum	5.68	93.7	12.93	14.22	1.18	41.45	41.78	1.16	1.09
Minimum	4.14	79.9	11.03	10.23	0.85	32.44	31.83	0.88	0.90
				Boys and Girls					
Average	4.98	84.9	11.72	11.83	0.99	35.75	36.03	1.00	0.99
Maximum	5.68	93.7	12.93	14.22	1.18	41.45	41.78	1.16	1.09
Minimum	4.14	76.5	10.56	10.23	0.85	32.44	31.83	0.88	0.88

TABLE 5.—*Results of Studies of the Blood of Boys and Girls 8 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	5.24	83.4	11.51	10.98	0.92	37.35	35.64	0.99	0.92
	4.82	82.1	11.33	11.75	0.98	32.01	33.20	0.92	1.06
	5.38	85.4	11.78	10.95	0.91	36.43	33.86	0.94	0.97
	4.97	86.6	11.95	12.02	1.00	37.34	37.57	1.04	0.96
	4.98	81.8	11.29	11.33	0.94	34.81	34.95	0.97	0.97
	4.80	84.9	11.72	12.20	1.02	36.39	37.90	1.05	0.97
	6.02	90.2	12.45	10.34	0.86	37.23	30.92	0.86	1.00
	4.60	92.8	12.81	13.92	1.16	37.72	41.00	1.14	1.02
	5.39	83.7	11.55	10.72	0.89	36.10	33.49	0.93	0.96
	4.61	73.0	10.07	10.93	0.91	31.55	34.22	0.95	0.96
	5.04	89.7	12.38	12.28	1.02	36.93	36.64	1.02	1.01
	5.27	90.8	12.53	11.89	0.99	38.94	36.95	1.03	0.97
	5.57	90.7	12.52	11.26	0.94	38.39	34.46	0.96	0.98
	5.48	85.2	11.76	10.73	0.89	37.32	34.05	0.95	0.95
	4.85	76.6	10.57	10.90	0.91	34.52	35.59	0.99	0.92
	5.46	84.5	11.66	10.68	0.89	37.79	34.61	0.96	0.93
Average	5.16	85.1	11.74	11.43	0.95	36.30	35.32	0.99	0.97
Maximum	6.02	92.8	12.81	13.92	1.16	38.94	41.00	1.14	1.06
Minimum	4.60	73.0	10.07	10.34	0.86	32.01	30.92	0.86	0.92
				Girls					
	4.71	84.4	11.65	12.36	1.03	34.09	36.19	1.01	1.03
	5.86	87.0	12.01	10.26	0.85	36.00	30.72	0.85	1.00
	5.58	92.3	12.74	11.41	0.95	38.55	34.54	0.96	0.99
	5.32	90.8	12.53	11.78	0.98	39.37	37.00	1.03	0.95
	4.43	77.2	10.65	12.02	1.00	32.78	37.00	1.03	0.98
	4.54	84.5	11.66	12.84	1.07	35.73	39.35	1.09	0.98
	4.89	82.3	11.36	11.61	0.97	35.35	36.15	1.00	0.96
	5.25	96.2	13.28	12.67	1.06	39.27	37.40	1.04	1.01
	4.66	85.0	11.73	12.59	1.05	38.27	41.17	1.14	0.92
Average	5.03	86.6	11.96	11.95	1.00	36.61	36.61	1.02	0.98
Maximum	5.86	96.2	13.28	12.84	1.07	39.37	41.17	1.14	1.03
Minimum	4.43	77.2	10.65	10.26	0.85	32.78	30.72	0.85	0.92
				Boys and Girls					
Average	5.11	85.6	11.82	11.62	0.97	36.41	35.78	0.99	0.97
Maximum	6.02	96.2	13.28	13.92	1.16	39.37	41.17	1.14	1.06
Minimum	4.43	73.0	10.07	10.26	0.85	32.01	30.72	0.85	0.92

TABLE 6.—*Results of Studies of the Blood of Boys and Girls 9 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	5.03	87.3	12.05	11.97	1.00	40.20	39.95	1.11	0.90
	4.83	71.4	9.85	10.20	0.85	32.45	33.59	0.93	0.91
	4.87	81.8	11.29	11.59	0.97	33.58	34.47	0.96	1.01
	4.96	83.4	11.51	11.60	0.97	35.25	35.54	0.99	0.98
	5.26	85.9	11.85	11.27	0.94	38.58	36.67	1.02	0.92
	5.24	77.5	10.69	10.21	0.85	35.35	33.73	0.94	0.91
	5.18	84.8	11.70	11.30	0.94	36.52	35.25	0.98	0.96
	5.13	78.4	10.82	10.55	0.88	34.22	33.25	0.93	0.95
	5.04	82.4	11.37	11.28	0.94	36.45	36.16	1.00	0.94
	5.44	81.3	11.22	10.31	0.86	35.28	32.43	0.90	0.95
	4.95	80.0	11.04	11.17	0.93	36.26	36.62	1.02	0.92
	5.12	82.4	11.37	11.10	0.93	38.16	37.27	1.04	0.89
	5.17	77.1	10.64	10.27	0.86	35.90	34.72	0.96	0.89
	5.12	80.0	11.04	10.78	0.90	35.23	34.41	0.96	0.94
Average	5.10	81.0	11.17	10.97	0.92	35.96	35.30	0.98	0.93
Maximum	5.44	87.3	12.05	11.97	1.00	40.20	39.95	1.11	1.01
Minimum	4.83	71.4	9.85	10.20	0.85	32.45	32.43	0.90	0.89
				Girls					
	5.45	92.0	12.70	11.65	0.97	37.71	34.60	0.96	1.01
	4.65	78.6	10.85	11.66	0.97	36.45	39.19	1.09	0.89
	4.92	87.0	12.01	12.20	1.02	35.85	36.43	1.01	1.00
	5.46	85.4	11.78	10.79	0.90	33.78	30.94	0.86	1.05
	5.13	95.8	13.22	12.89	1.07	38.46	37.49	1.04	1.03
	4.54	77.9	10.75	11.84	0.99	34.39	37.87	1.05	0.94
	4.64	88.0	12.14	13.09	1.09	35.75	38.52	1.07	1.02
	4.86	85.2	11.76	12.10	1.01	34.72	35.72	0.99	1.02
	4.84	84.7	11.69	12.07	1.01	37.17	38.40	1.07	0.94
	5.20	85.5	11.80	11.35	0.95	37.20	35.77	0.99	0.95
Average	4.97	86.0	11.87	11.96	1.00	36.15	36.49	1.01	0.99
Maximum	5.45	95.8	13.22	13.09	1.09	38.46	39.19	1.09	1.05
Minimum	4.54	77.9	10.75	10.79	0.90	33.78	30.94	0.86	0.89
				Boys and Girls					
Average	5.04	83.1	11.47	11.39	0.95	36.04	35.80	0.99	0.95
Maximum	5.45	95.8	13.22	13.09	1.09	40.20	39.95	1.11	1.05
Minimum	4.54	71.4	9.85	10.20	0.85	32.45	30.94	0.86	0.89

TABLE 7.—*Results of Studies of the Blood of Boys and Girls 10 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	5.14	93.2	12.86	12.51	1.04	36.43	35.44	0.98	1.08
	4.99	86.8	11.98	12.00	1.00	35.41	35.48	0.99	1.01
	5.38	87.0	12.01	11.16	0.93	38.61	35.88	1.00	0.93
	4.88	93.2	12.86	13.18	1.10	36.87	37.77	1.05	1.05
	6.16	103.1	14.23	11.55	0.96	39.42	31.99	0.89	1.08
	4.75	81.5	11.25	11.84	0.99	34.03	35.82	1.00	0.99
	5.06	102.6	14.16	13.99	1.17	40.19	39.71	1.10	1.06
	4.52	72.9	10.06	11.13	0.93	33.41	36.96	1.03	0.90
	5.10	84.5	11.66	11.43	0.95	37.50	36.76	1.02	0.93
	5.46	90.8	12.53	11.47	0.96	40.44	37.03	1.03	0.93
Average	5.14	89.6	12.36	12.03	1.00	37.23	36.28	1.01	0.99
Maximum	6.16	103.1	14.23	13.99	1.17	40.44	39.71	1.10	1.06
Minimum	4.52	72.9	10.06	11.13	0.93	33.41	31.99	0.89	0.93
				Girls					
	5.03	93.4	12.89	12.81	1.07	36.06	35.84	1.00	1.07
	5.02	91.3	12.60	12.55	1.05	37.26	37.11	1.03	1.01
	5.02	84.5	11.66	11.61	0.97	38.07	38.01	1.06	0.92
	4.97	89.2	12.31	12.38	1.03	36.19	36.40	1.01	1.02
	4.61	77.8	10.74	11.64	0.97	33.65	36.50	1.01	0.96
	4.38	86.1	11.88	13.56	1.13	36.41	41.56	1.15	0.98
	4.76	86.9	11.99	12.60	1.05	35.90	37.71	1.05	1.00
	5.15	95.8	13.22	12.84	1.07	39.27	38.13	1.06	1.01
	5.47	103.7	14.31	13.08	1.09	42.38	38.74	1.08	1.01
	5.08	96.7	13.34	13.13	1.09	39.86	39.23	1.09	1.00
Average	4.95	90.5	12.49	12.62	1.05	37.51	37.92	1.05	1.00
Maximum	5.47	103.7	14.31	13.56	1.13	42.38	41.56	1.15	1.07
Minimum	4.38	77.8	10.74	11.61	0.97	38.65	35.84	1.00	0.92
				Boys and Girls					
Average	5.05	90.1	12.43	12.32	1.03	37.37	37.10	1.03	1.00
Maximum	6.16	103.7	14.31	13.99	1.17	42.38	41.56	1.15	1.07
Minimum	4.38	72.9	10.06	11.13	0.93	33.41	31.99	0.89	0.92

TABLE 8.—*Results of Studies of the Blood of Boys and Girls 11 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	5.66	88.7	12.24	10.81	0.90	40.57	35.84	1.00	0.91
	5.57	91.1	12.57	11.29	0.94	37.95	34.06	0.95	0.99
	5.23	85.3	11.77	11.25	0.94	35.01	33.47	0.93	1.01
	5.28	94.2	13.00	12.31	1.03	38.61	36.56	1.02	1.01
	5.15	79.1	10.92	10.60	0.88	35.42	34.39	0.96	0.92
	5.18	90.8	12.53	12.10	1.01	39.13	37.77	1.05	0.96
	5.09	88.4	12.20	11.98	1.00	36.01	35.37	0.98	1.02
	4.97	85.8	11.84	11.91	0.99	36.54	36.76	1.02	0.97
	4.74	89.0	12.28	12.96	1.08	36.28	38.27	1.06	1.02
	5.06	101.5	14.01	13.84	1.15	36.12	35.69	0.99	1.16
Average	5.19	89.4	12.34	11.91	0.99	37.16	35.82	1.00	1.00
Maximum	5.66	101.5	14.01	13.84	1.15	40.57	38.27	1.06	1.16
Minimum	4.74	79.1	10.92	10.60	0.88	35.01	33.47	0.93	0.91
				Girls					
	5.65	84.3	11.63	10.30	0.86	34.70	30.71	0.85	1.01
	4.99	84.9	11.72	11.74	0.98	37.56	37.64	1.05	0.94
	5.60	92.3	12.74	11.37	0.95	37.08	33.11	0.92	1.03
	5.56	88.2	12.17	10.95	0.91	39.81	35.80	0.99	0.92
	5.19	83.6	11.56	11.11	0.93	34.40	33.14	0.92	1.01
	4.37	78.4	10.82	12.38	1.03	32.77	37.50	1.04	0.99
	4.99	88.9	12.27	12.29	1.02	37.98	38.06	1.06	0.97
	4.99	93.6	12.92	12.94	1.08	33.85	33.92	0.94	1.14
	4.43	76.6	10.57	11.93	0.99	30.70	34.65	0.96	1.03
	5.36	84.8	11.70	10.92	0.91	36.00	33.58	0.93	0.98
	4.68	87.1	12.02	12.84	1.07	39.12	41.79	1.16	0.92
Average	5.07	85.7	11.83	11.76	0.97	35.82	35.45	0.98	0.99
Maximum	5.65	93.6	12.74	12.94	1.08	39.81	41.79	1.16	1.14
Minimum	4.37	76.6	10.57	10.30	0.86	30.70	30.71	0.85	0.92
				Boys and Girls					
Average	5.13	87.5	12.07	11.80	0.98	36.46	35.64	0.99	1.00
Maximum	5.66	101.5	14.01	13.84	1.15	40.57	41.79	1.16	1.16
Minimum	4.37	76.6	10.57	10.30	0.86	30.70	30.71	0.85	0.91

TABLE 9.—*Results of Studies of the Blood of Boys and Girls 12 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	5.60	95.2	13.14	11.73	0.98	39.28	35.16	0.98	1.00
	5.80	90.3	12.46	10.74	0.89	40.97	35.32	0.98	0.91
	5.23	98.0	13.52	12.98	1.08	36.71	35.10	0.97	1.11
	5.13	81.9	11.30	11.02	0.92	35.41	34.51	0.96	0.96
	4.94	90.6	12.50	12.66	1.06	37.17	37.62	1.04	1.01
	5.27	92.1	12.71	12.06	1.00	37.68	35.75	0.99	1.01
	5.06	88.3	12.19	12.04	1.00	38.37	37.91	1.05	0.95
	5.63	81.1	11.19	9.94	0.83	36.83	32.71	0.91	0.91
	4.78	85.9	11.85	12.40	1.03	36.04	37.70	1.05	0.99
	4.66	84.5	11.66	12.51	1.04	35.59	38.19	1.06	0.98
Average	5.21	88.8	12.25	11.80	0.98	37.41	36.00	1.00	0.98
Maximum	5.80	98.0	13.52	12.98	1.08	40.97	38.19	1.06	1.11
Minimum	4.66	81.1	11.19	9.94	0.83	35.41	32.71	0.91	0.91
				Girls					
	5.22	86.1	11.88	11.38	0.95	35.80	34.29	0.95	1.00
	4.56	88.4	12.20	13.38	1.12	35.41	38.83	1.08	1.03
	4.96	82.0	11.32	11.41	0.95	33.81	34.09	0.95	1.00
	4.95	84.3	11.63	11.75	0.98	33.25	33.59	0.93	1.05
	5.24	94.4	13.03	12.43	1.04	37.44	35.73	0.99	1.04
	5.26	87.9	12.13	11.53	0.96	36.04	34.26	0.95	1.01
	5.34	92.8	12.81	11.99	1.00	37.86	35.45	0.98	1.01
	5.35	91.7	12.65	11.83	0.99	38.31	35.80	0.99	0.99
	5.08	82.4	11.37	11.19	0.93	35.47	34.91	0.97	0.96
	4.47	79.8	11.01	12.32	1.03	33.81	37.82	1.05	0.98
Average	5.04	87.0	12.00	11.92	0.99	35.72	35.48	0.98	1.01
Maximum	5.35	94.4	13.03	13.38	1.12	38.31	38.83	1.08	1.05
Minimum	4.47	79.8	11.01	11.19	0.93	33.25	33.59	0.93	0.96
				Boys and Girls					
Average	5.13	87.9	12.13	11.86	0.99	36.57	35.73	0.99	1.00
Maximum	5.80	98.0	13.52	13.38	1.12	40.97	38.83	1.08	1.11
Minimum	4.47	79.8	11.01	9.94	0.83	33.25	32.71	0.91	0.91

TABLE 10.—*Results of Studies of the Blood of Boys and Girls 13 Years Old*

	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
		Percentage	Grams						
				Boys					
	5.50	95.4	13.17	11.79	0.98	36.54	33.22	0.92	1.08
	5.76	99.0	13.66	11.86	0.99	41.47	36.00	1.00	0.99
	5.43	101.9	14.06	12.95	1.08	39.75	36.60	1.02	1.06
	6.08	107.9	14.92	12.27	1.02	46.51	38.25	1.06	0.96
	4.88	90.0	12.42	12.73	1.06	36.58	37.48	1.04	1.02
	5.27	89.8	12.39	11.76	0.98	31.88	30.24	0.84	1.17
	4.10	75.1	10.37	12.64	1.05	30.37	37.04	1.03	1.02
	5.57	93.3	12.88	11.56	0.96	38.39	34.46	0.96	1.01
	5.38	93.2	12.86	11.95	1.00	38.86	36.12	1.00	0.99
	5.05	88.1	12.16	12.04	1.00	37.32	36.95	1.03	0.98
Average	5.30	93.4	12.89	12.16	1.01	37.77	35.64	0.99	1.03
Maximum	6.08	107.9	14.92	12.95	1.08	46.51	38.25	1.06	1.17
Minimum	4.10	75.1	10.37	11.56	0.96	30.37	30.24	0.84	0.96
				Girls					
	4.91	101.4	13.99	14.25	1.19	41.05	41.80	1.16	1.02
	5.49	92.1	12.71	11.58	0.96	39.14	35.65	0.99	0.97
	5.44	98.7	13.62	12.52	1.04	43.00	39.52	1.10	0.95
	4.74	90.2	12.45	13.13	1.09	36.87	38.89	1.08	1.01
	4.96	89.6	12.36	12.47	1.04	38.21	38.52	1.07	0.97
	5.44	98.7	13.62	12.52	1.04	39.42	36.23	1.01	1.04
	4.95	81.3	11.22	11.33	0.94	37.29	37.67	1.05	0.90
	4.96	85.7	11.83	11.92	0.99	36.45	36.75	1.02	0.97
	5.57	107.3	14.81	13.29	1.11	34.31	30.80	0.86	1.29
	4.86	91.1	12.57	12.93	1.08	37.56	38.64	1.07	1.00
Average	5.13	93.6	12.92	12.57	1.05	38.33	37.48	1.04	1.01
Maximum	5.57	107.3	14.81	14.25	1.19	43.00	41.80	1.16	1.29
Minimum	4.47	81.3	11.22	11.33	0.94	34.31	30.80	0.86	0.90
				Boys and Girls					
Average	5.22	93.5	12.90	12.37	1.03	38.05	36.54	1.02	1.02
Maximum	6.08	107.9	14.92	14.95	1.19	46.51	41.80	1.16	1.29
Minimum	4.10	75.1	10.37	11.33	0.94	30.37	30.24	0.84	0.90

RESULTS

The detailed results of our studies are presented in tables 2 to 10 and are summarized in table 11. It is noteworthy that there was no significant variation with sex or age in any of the values reported for the entire group. This makes it possible to use the averages and ranges of variation calculated from the total group of 215 children as normal standards with which to compare examinations of the blood of any

TABLE 11.—*Summary of Results of Studies of the Blood of Boys and Girls from 4 to 13 Years of Age*

Age	No.	Red Blood Cells, Millions	Hemoglobin		Hemoglobin Coefficient	Color Index	Cell Volume, Cc. per 100 Cc.	Volume Coefficient	Volume Index	Saturation Index
			Percentage	Grams						
					Boys					
4	11	4.81	80.7	11.14	11.68	0.97	33.38	34.89	0.97	1.00
5	11	4.92	84.0	11.59	11.83	0.99	34.86	35.58	0.99	1.00
6	9	5.00	84.1	11.61	11.74	0.98	34.61	34.87	0.97	1.01
7	11	4.92	82.6	11.40	11.62	0.97	35.49	36.14	1.00	0.96
8	16	5.16	85.1	11.74	11.43	0.95	36.30	35.32	0.99	0.97
9	14	5.10	81.0	11.17	10.97	0.92	35.96	35.30	0.98	0.93
10	10	5.14	89.6	12.36	12.03	1.00	37.23	36.28	1.01	0.99
11	10	5.19	89.4	12.34	11.91	0.99	37.16	35.82	1.00	1.00
12	10	5.21	88.8	12.25	11.80	0.98	37.41	36.00	1.00	0.98
13	10	5.30	93.4	12.89	12.16	1.01	37.77	35.64	0.99	1.03
Aver.	112	5.07	84.7	11.81	11.67	0.97	36.00	35.56	0.99	0.99
Maximum		6.16	107.9	14.92	14.62	1.22	46.51	41.00	1.14	1.17
Minimum		4.10	68.2	9.41	9.35	0.78	28.76	29.96	0.83	0.87
					Girls					
4	10	4.96	88.5	12.21	12.33	1.03	35.12	35.56	0.99	1.04
5	10	4.83	81.7	11.28	11.75	0.98	33.90	35.22	0.98	1.00
6	13	4.94	85.4	11.78	11.95	1.00	35.49	36.01	1.00	1.00
7	10	5.04	87.5	12.08	12.06	1.00	36.04	35.92	1.00	1.01
8	9	5.03	86.6	11.96	11.95	1.00	36.61	36.61	1.02	0.98
9	10	4.97	86.0	11.87	11.96	1.00	36.15	36.49	1.01	0.99
10	10	4.95	90.5	12.49	12.62	1.05	37.51	37.92	1.05	1.00
11	11	5.07	85.7	11.83	11.76	0.97	35.82	35.45	0.98	0.99
12	10	5.04	87.0	12.00	11.92	0.99	35.72	35.48	0.98	1.01
13	10	5.13	93.6	12.92	12.57	1.05	38.33	37.48	1.04	1.01
Aver.	103	5.00	87.2	12.03	12.08	1.01	36.04	36.19	1.01	1.00
Maximum		5.86	107.3	14.81	14.25	1.32*	43.00	41.80	1.16	1.29*
Minimum		4.06	71.7	9.89	10.02	0.83	30.70	30.71	0.85	0.89
					Boys and Girls					
Aver.	215	5.04	85.9	11.92	11.87	0.99	36.02	35.87	1.00	0.99
Maximum		6.16	107.9	14.92	14.62	1.32*	46.51	41.80	1.16	1.29*
Minimum		4.06	68.2	9.41	9.35	0.78	28.76	29.96	0.83	0.87

* This high figure is probably due to a technical error; but since the subjects could not be located to repeat the determinations they have been retained.

child of either sex and of any age from 4 to 13, inclusive. The range, which includes 95 per cent of the cases and corresponds to ± 3 probable errors, is recommended as the one for use in clinical interpretation. Since these values differ from those determined for other ages,[10] they are not applicable to infants, adolescents or adults.

The frequency distribution of our data is shown in charts 1 to 6. In most instances the average is also the most frequently occurring figure and the configuration corresponds satisfactorily to a probability curve.

10. Osgood, E. E.: Normal Hematologic Standards, Arch. Int. Med., to be published.

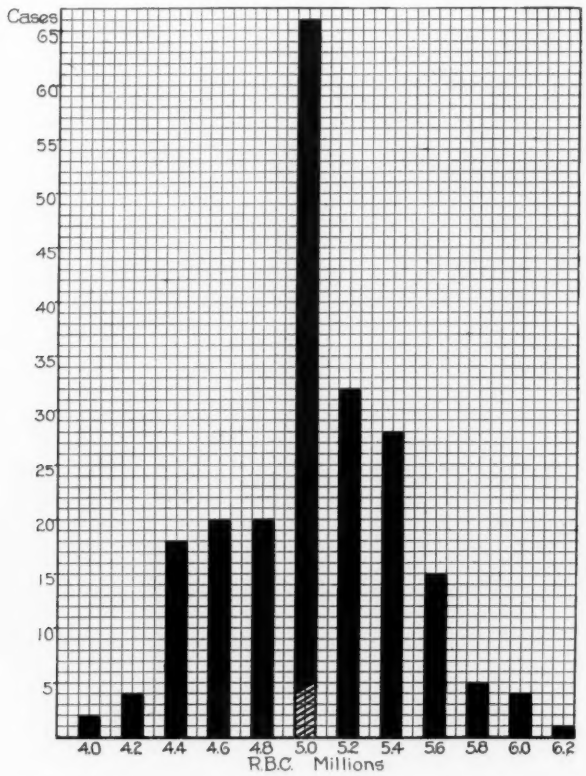

Chart 1.—Frequency distribution of red blood cell counts.

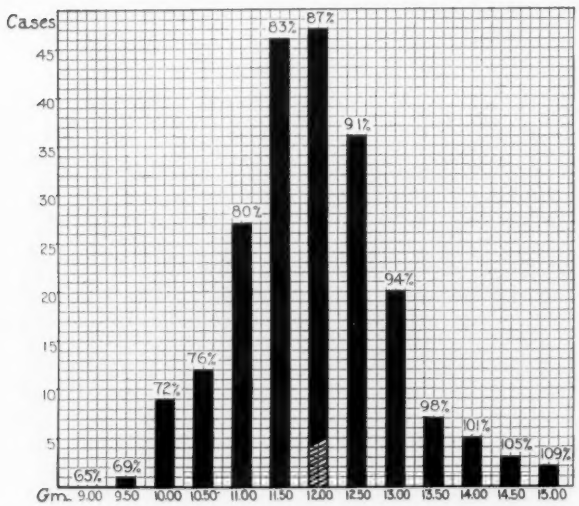

Chart 2.—Frequency distribution of hemoglobin concentrations.

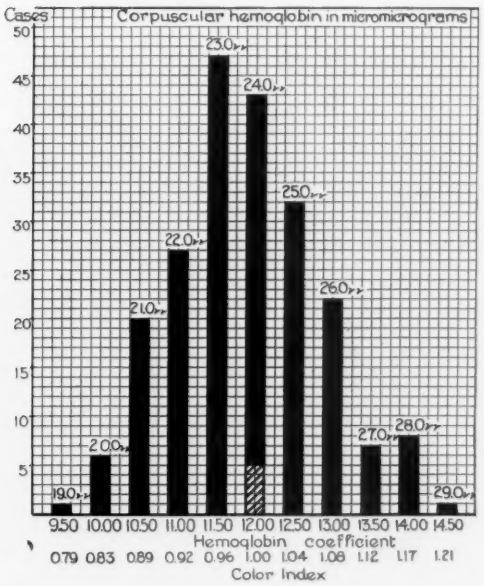

Chart 3.—Frequency distribution of color indexes, hemoglobin coefficients and corpuscular hemoglobin concentrations.

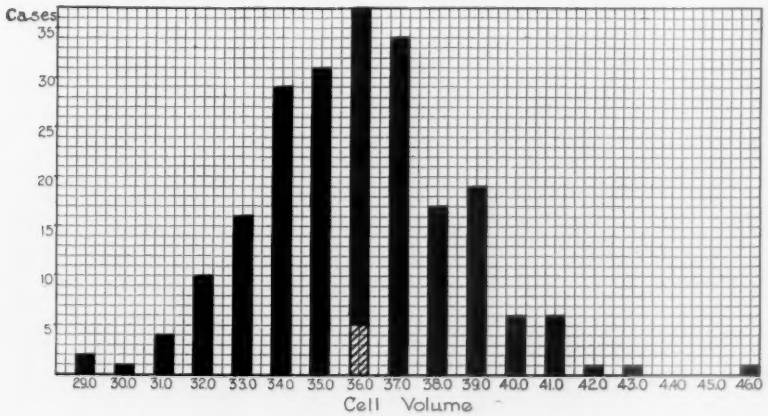

Chart 4.—Frequency distribution of red cell volumes.

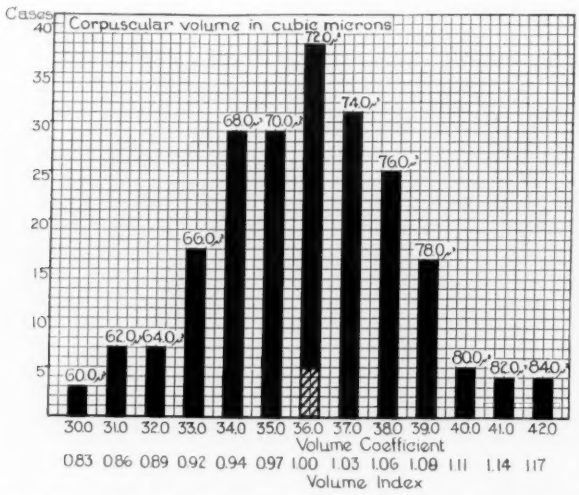

Chart 5.—Frequency distribution of volume indexes, volume coefficients and corpuscular volumes.

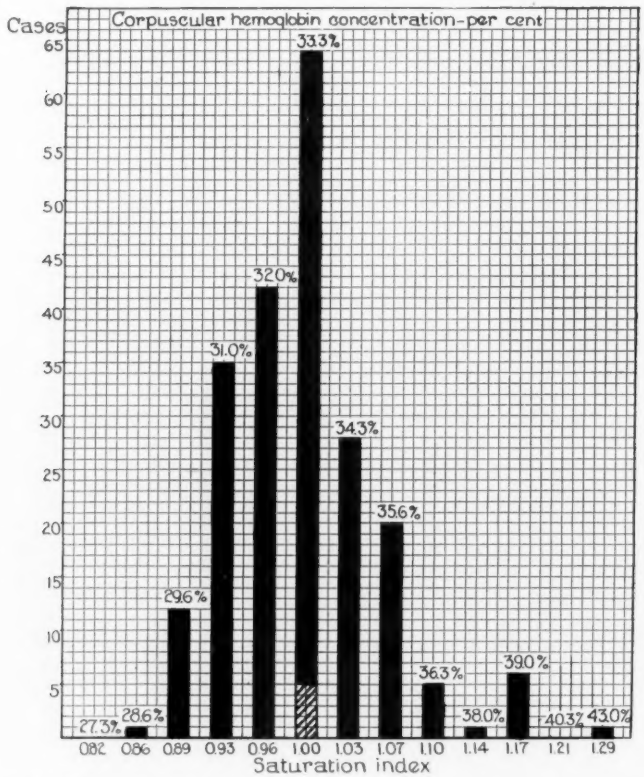

Chart 6.—Frequency distribution of saturation indexes and corpuscular hemoglobin concentrations.

The average red cell count (table 11 and chart 1) is 5,000,000 (5,040,000).[11] This is lower than the average figure of 5,400,000 found for males [12] over 13 years of age and higher than the average figure of 4,800,000 for females [12] over 13. The extreme range is from 4,060,000 to 6,160,000, and 95 per cent of the results are between 4,200,000 and 5,800,000.

The average hemoglobin content (table 11 and chart 2) is 12 (11.92) Gm. per hundred cubic centimeters, which is lower than that of 13.8 Gm. found for females [12] over 13 years of age and much lower than the average of 15.8 Gm. for males [12] over 13. The extreme range is from 9.41 to 14.92 Gm., and 95 per cent of the results are between 10 and 14 Gm.

The hemoglobin coefficient (table 11 and chart 3) averages 12 (11.87) Gm. and ranges from 9.35 to 14.62 Gm., with 95 per cent of the results between 10.2 and 13.8 Gm. The average is lower than the value of 14.3 Gm. obtained for females [12] over 13 years of age and of 14.7 Gm. obtained for males [12] over 13 years.

The color index averages 1.00 (0.99) and ranges from 0.78 to 1.22 (1.32) with 95 per cent of the results between 0.85 and 1.15. As may be seen in figure 4, the hemoglobin coefficient, color index and corpuscular hemoglobin are three ways of expressing the relation between the red blood cell count and the hemoglobin.

The cell volume (table 9 and chart 4) is also lower than in older males and females,[12] averaging 36 (36.02) cc. per hundred cubic centimeters of blood as compared with 41 cc. for females over 17 years of age and boys from 14 to 19 and 45 cc. for men 20 years of age and older. The extreme range is from 28.76 to 46.51 cc., with 95 per cent of the values between 31 and 41 cc.

The volume coefficient (table 11 and chart 5) averages 36 (35.87), and shows an extreme range from 29.96 to 41.8, with 95 per cent of the results between 31 and 41. The average is lower than that of 41 for men [12] and 43 for women,[12] indicating that children have definitely smaller red blood cells than adults.

The volume index averages 1.00 (1) and shows an extreme range from 0.83 to 1.16, with 95 per cent of the results between 0.85 and 1.15. As may be seen in chart 4, the volume coefficient, volume index and corpuscular volume are three ways of expressing the relation between the red blood cell count and the cell volume.

The saturation index averages 1.00 (0.99) and shows an extreme range from 0.87 to 1.19 (1.29), with 95 per cent of the results between 0.9 and 1.1. As may be seen in chart 6, the corpuscular hemoglobin concentration is another way of expressing the relation between cell

11. The figures given in parenthesis are the actual averages.

12. Osgood and Haskins.[2b] Osgood.[2c] Osgood.[10]

volume and hemoglobin. Comparison with the figures for other age groups [10] indicates that there is little or no variation with age or sex in the corpuscular hemoglobin concentration.

We have summarized the estimations of the red cell counts and the results of the determinations of hemoglobin content in the literature in

TABLE 12.—*Résumé of Blood Studies Reported in the Literature*

Author	Place	Number	Age	Red Blood Cells, Millions	Hemoglobin* Percentage	Hemoglobin* Grams	Method
Sörenson: Antalet af röde og hvide Blodlegemer under forskjellige tilstande, Copenhagen, 1876	Denmark	4	5	5.03			
Bouchut and Dubrisay: Gaz. méd. de Paris **7**: 168, 1878...	France	?	2.5 to 15	4.27†			
Leichtenstern: Hämoglobulingehalt d. Blutes in gesunden u. kranken Zuständen, Leipzig, F. C. W. Vogel, 1878	Germany	31	4 to 15	....	..	11.60	Spectrophotometer
Widowitz: Jahrb. f. Kinderh. **27**: 380, 1888	Germany	20	4 to 10	5.27	86	(13.59)	Fleischl
Stierlin: Deutsches Arch. f. klin. Med. **45**: 75, 1889.....	Germany	20	4 to 10	....	80	(12.64)	Fleischl (?)
Carstanjen: Jahrb. f. Kinderh. **52**: 215, 333 and 648, 1900	Germany	42	4 to 13	....	72	(11.30)	Fleischl
Perlin: Jahrb. f. Kinderh. **57**: 549, 1903	Switzerland	43	4 to 13	5.00	77	(12.20)	Fleischl
Williamson: Arch. Int. Med. **18**: 505 (Oct.) 1916.....	Chicago	99	4 to 10	....	..	13.79 (12.41)	Spectrophotometer
Als: Nord. med. Ark. **58**: 62, 1923	Denmark	82	7 to 13	5.31			
Sobel and Drektor: Am. J. Dis. Child. **45**: 486 (March) 1933	New York	48	?	4.95	..	13.10	Blood iron
Goldhamer and Fritzell: J. Lab. & Clin. Med. **19**: 172, 1933	Ann Arbor, Mich.	41	12 to 13	4.70	..	11.18	Sahli
Total		239 344		5.07		12.2	
Osgood and Baker, 1934.....	Portland, Ore.	215	4 to 13	5.04	..	11.92	Osgood-Haskins
All		454 559		5.05		12.08	

* The figures in parenthesis were calculated.
† This figure was not included in the average.

table 12. Since no differences in sex were noted by the workers the results for the sexes have been averaged. The average red cell count of 5.07 for the 239 subjects previously reported on agrees well with the average of 5.04 for the 215 subjects reported on here. After correcting for known errors in the methods used for the estimation of hemoglobin the average hemoglobin content of 12.2 Gm. per hundred cubic centi-

meters for the 344 subjects previously reported on agrees as well as could be expected with the average for our 215 subjects. No reports on cell volume, volume or saturation index determinations for this age group were found.

COMMENT

Our studies indicate that the red blood cells of children are smaller than those of adults and contain less hemoglobin. The concentration of hemoglobin per unit volume of erythrocytes is the same, however. The average normal hemoglobin coefficients differ so markedly with age and sex that no one figure is correct as 100 per cent. For this reason and because the methods in common use have different values for 100 per cent, it is advisable to report values for hemoglobin as grams per hundred cubic centimeters rather than as percentages.

Polycythemia in children from 4 to 13 years of age is present if the red blood cell count or hemoglobin content or both are significantly greater than 5,800,000 or 14 Gm., respectively.

Anemia is present in children if the red cell count or hemoglobin content or both are significantly lower than 4,200,000 or 10 Gm., respectively. If anemia is present its type should be determined by calculation of the color, volume and saturation indexes. Although little work has been done on anemia in childhood, studies on adults [13] have resulted in a classification which will probably prove applicable to anemia in childhood. In macrocytic anemia the color and volume indexes are above 1.15 and the saturation index is normal. Anemia of this type responds to treatment with the active principle of liver or stomach. Patients with normocytic and simple microcytic anemia have, respectively, normal or low color and volume indexes and a normal saturation index. The treatment of these types of anemia consists of finding and removing the cause. Neither liver nor iron is beneficial, but transfusions of blood often help. Microcytic hypochromic anemia is characterized by color and volume indexes below 0.85 and a saturation index below 0.90. The cause of this type is usually chronic hemorrhage, deficient iron in the diet or achlorhydria resulting in deficient absorption of iron. Iron in large doses is the specific treatment. A diagnosis of "secondary anemia" is never adequate,[13a] since it does not indicate the type, the etiology or the treatment of the anemia.

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13. (*a*) Haden, R. L.: Accurate Criteria for Differentiating Anemias, Arch. Int. Med. **31**:766 (May) 1934. Osgood, E. E.; Haskins, H. D., and Trotman, F. E.: The Value of Accurately Determined Color, Volume and Saturation Indexes in Anemias, J. Lab. & Clin. Med. **17**:859 (June) 1932. Osgood, E. E., and Haskins, H. D.: Causes, Classification and Differential Diagnosis of Anemias, Ann. Int. Med. **5**:1367 (May) 1932. Wintrobe, M. M.: Anemia: Classification and Treatment on the Basis of Differences in the Average Volume and Hemoglobin Content of the Red Corpuscles, Arch. Int. Med. **54**:256 (Aug.) 1934. (*b*) Osgood and Haskins.[2b] Osgood.[2c]

SUMMARY

Hematologic examinations are reported on the oxalated venous blood of 112 healthy boys and 103 healthy girls, aged from 4 to 13 years, inclusive.

The accurate methods used in making these examinations are briefly discussed.

There were no significant differences in these hematologic examinations with age or sex in this group.

The following values are recommended as normal for children of this age:

	Average	95 Per Cent Range
Erythrocyte count, millions	5	4.20 to 5.80
Hemoglobin, grams	12	10.00 to 14.00
Hemoglobin coefficient	12	10.20 to 13.80
Cell volume, cc	36	31.00 to 41.00
Volume coefficient	36	31.00 to 41.00
Color index	1	0.85 to 1.15
Volume index	1	0.85 to 1.15
Saturation index	1	0.90 to 1.10

The results in these 215 children agree satisfactorily with those summarized from the literature.

The application of these normal standards to the diagnosis and treatment of anemia in children are discussed.

CHRONIC GALACTEMIA

REPORT OF CASE WITH STUDIES ON CARBOHYDRATES

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AND

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The purpose of this paper is to report an instance of prolonged galactosuria associated with disturbance of nutrition and development in which studies on carbohydrates were carried out over a considerable period of time with findings that appear to throw light on the character of the disturbance.

Digestion, in preparing the usable carbohydrate of the diet for absorption, converts most of it into three monosaccharides (dextrose, levulose and galactose), and as such it passes into the blood of the portal circulation. The three monosaccharides as such are not utilized with equal facility by the tissues, for while dextrose is burned readily, levulose is used less easily, and galactose is consumed in very small amounts or not at all. However, before reaching the general circulation and becoming available to the tissues of the body, all these materials must pass through the liver, a passage which is supposed to result in the conversion into dextrose—probably through synthesis and the subsequent breakdown of glycogen—of the sugars which are less well adapted to the needs of the tissues. During infancy, when lactose forms a large part of the ingested carbohydrate, the successful conversion of galactose into the more readily utilized dextrose is of particular importance. The evidence is strong that the conversion takes place almost exclusively, if not entirely, in the liver. Draudt [1] found that a dog with an Eck fistula excreted the larger part, in one instance 79 per cent, of the ingested galactose.

Since Bauer [2] in 1906 suggested the application of galactose tolerance as a test of hepatic function, considerable data bearing on the subject have accumulated. A normal adult ordinarily ingests from 30 to 40 Gm. of galactose, and most normal children between 2 and 5

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Read in part at the meeting of the Federation of American Societies for Experimental Biology at New York, March 30, 1934, and at the meeting of the Society for Pediatric Research at Atlantic City, May 1, 1934.

1. Draudt, L.: Arch. f. exper. Path. u. Pharmakol. **72**:457, 1913.
2. Bauer, R.: Wien. med. Wchnschr. **56**:2538, 1906.

years of age ingest from 15 to 20 Gm., without exhibiting more than slight galactosuria. If, however, the liver is damaged, the tolerance for galactose falls, and it seems that the percentage of ingested galactose that is excreted in the urine varies directly with the extent of the lesion in the hepatic parenchyma. Thus, the highest percentage is excreted in the diseases with diffuse involvement of the parenchyma of the liver, such as acute yellow atrophy and catarrhal jaundice; a smaller percentage, in conditions with less diffuse lesions, such as cirrhosis, and usually none, in biliary obstructions due to stone, unless of long standing.

It is clear, then, that the normal liver possesses a limited ability to convert galactose into dextrose and that the rate of conversion cannot keep pace with the potential rate of absorption from the intestine. When the absorption is rapid, a part of the galactose passes the liver and enters the general circulation. When the galactose-converting function of the liver is impaired, the amount of galactose which finds its way into the circulation is increased, and under ordinary circumstances any considerable amount of galactose in the general circulation is thought to give rise to galactosuria. Now and again patients are encountered who appear to be unable to take even ordinary amounts of milk without excreting galactose in quantity. In these patients the disturbance is usually either temporary or rapidly fatal, and detailed studies of carbohydrate metabolism or of the effect on the organism of the long continued presence of galactose in the blood are not feasible.

During the past two and one-half years we have had under continuous observation a patient who exhibited marked intolerance for galactose. We have been able to discover a report of only one comparable case in the literature, that of Göppert,[3] in 1917. An abstract of this case follows.

The patient was 2 years and 5 months of age when he came under observation. He was the fourth of four children. At birth the liver was large, and a few days after birth a severe icterus developed, which lasted until he was 8 months of age. The Wassermann reaction of the blood was always negative. He received human milk almost entirely until 7 months of age, when his food was changed to a cow's milk mixture. He gained slowly until 9 months of age, when he became ill after a dose of mild mercurous chloride. At 1 year of age he had scurvy, and at 1½ years he was said to have had nephritis after a dose of mild mercurous chloride.

At 2 years and 5 months the weight was 6,260 Gm. (13 pounds, 12 ounces), and the mental and physical development was that of a child of from 6 to 8 months of age. He neither talked nor walked, but he showed no signs of rickets. The spleen was palpable 2 cm. below the costal margin, and the liver reached the iliac crest and extended down 10 cm. in the mammary line. The edge of the liver was hard and sharp. The urine gave a positive reaction for albumin and sugar; from 0.3 to 0.8 per cent of sugar was present most of the time. In the morning the percentage was usually low. This reducing substance was finally determined to be galactose. It was then found that the amount of sugar in the urine could

3. Göppert, F.: Berl. klin. Wchnschr. **54**:473, 1917.

be lowered by reducing the amount of milk fed. When the patient was put on an almost milk-free diet he began to gain at once, and after nine months he weighed 10,700 Gm. (23 pounds and 8 ounces). Sugar and albumin had disappeared from the urine; the liver was considerably smaller; the spleen could no longer be felt, and the child walked and talked a little.

At this time the tolerance for sucrose, maltose, levulose and dextrose was normal, but the ingestion of from 10 to 20 Gm. of galactose or lactose led to the excretion of sugar in the urine. The excretion began almost immediately and lasted for about eight hours. Later it was found that the child could take 15 Gm. of lactose without excreting sugar but that 25 Gm. caused an excretion of galactose.

Our patient came under observation when younger than that of Göppert and has been studied for a longer period.

REPORT OF CASE

History.—T. B., a Negro boy, the sixth of seven children, was born in the Sloane Hospital on March 5, 1931. Labor terminated in a spontaneous breech delivery. The child was markedly asphyxiated, and respiration and crying were delayed. His weight at birth was 4,090 Gm. (9 pounds). For seven days he was nursed only. Then a supplementary feeding of cow's milk, water and sucrose was given after each nursing. He was discharged on the eleventh day, weighing 3,750 Gm. (8 pounds and 4 ounces). Failure to gain while in the hospital may well have been due to insufficient food. There was no history of jaundice or of enlargement of the liver or spleen. When 7 weeks old he had pneumonia but was treated at home.

He was not seen again until Sept. 14, 1931, when he was admitted to the Babies Hospital at 6 months of age because of failure to gain, fever for three weeks and vomiting. His mother stated that he had always been difficult to feed and that he frequently regurgitated a considerable amount after being fed. The bowels had moved regularly, and the stools had been normal except during a short attack of diarrhea at 5½ months of age. The child was taking 5 ounces (147.9 cc.) of the following mixture: milk, 23 ounces (680.1 cc.); water, 12 ounces (354.8 cc.); dextrimaltose, 5 tablespoonfuls. Orange and tomato juice had been begun at 1 month of age, and on his admission he was taking 1 ounce (29.57 cc.) a day. Cod liver oil had been started at 7 weeks, and on admission he was said to be taking 5 teaspoonfuls a day.

Family History.—There was no family history of tuberculosis, nephritis or diabetes. The father was 36 and was said to have had syphilis. The mother was 37 and was well except for mild chronic arthritis. The Wassermann test of the mother's blood, made during each pregnancy, always gave a negative reaction. The first three children, a girl of 14, a boy of 13 and a girl of 12, were alive and well. The fourth child, a girl, died when 5 months of age of an unknown cause. The fifth, a girl, died when 13 months of age of pneumonia and otitis. The seventh child, born a year and a half after the patient, was apparently in normal health when 3 months old. None of the children living showed disturbance of nutrition or enlargement of the liver or spleen.

Physical Examination.—The infant was small for his age, and the abdomen was prominent. He did not look acutely ill but took little interest in his surroundings. The mucous membranes were pale, and the conjunctivae were subicteric. He had a mild infection of the upper respiratory tract, bilateral otitis media and enlarged tonsils. The cervical, axillary and epitrochlear lymph nodes were slightly enlarged.

The liver was markedly enlarged, reaching the iliac crest in the right flank. The spleen was palpable 2 cm. below the costal margin. Both the liver and the spleen were smooth and firm. The child weighed 5,057 Gm. (11 pounds and 4 ounces). The measurements were as follows: height, 62.5 cm. (24.6 inches); length from scalp to umbilicus, 33 cm. (12.9 inches); length from umbilicus to sole, 29 cm. (11.4 inches); circumference of the head, 40.6 cm. (15.9 inches); circumference of the chest, 37 cm. (14.5 inches); circumference of the abdomen, 39.4 cm. (15.5 inches).

Laboratory Findings.—Examination of the blood showed moderate anemia, the blood count on admission to the hospital being as follows: hemoglobin, 9.4 Gm. per hundred cubic centimeters; red cells, 2,952,000; white cells, 13,000; polymorphonuclears, 57 per cent; lymphocytes, 41 per cent; mononuclears, 1 per cent; eosinophils, 1 per cent. The sedimentation rate was normal. The van den Bergh test on the blood serum was made four times while the child was in the hospital.

Blood Chemistry Values Obtained for Patient with Chronic Galactemia *

Age of Patient	Date	Nonprotein Nitrogen, Mg. per 100 Cc.	Chlorides (as Sodium Chloride), Mg. per 100 Cc.	Sugar, Mg. per 100 Cc.	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Combining Power of Carbon Dioxide, Volumes per Cent	Cholesterol, Mg. per 100 Cc.	Albumin, Gm. per 100 Cc.	Globulin, Gm. per 100 Cc.	Fibrinogen, Gm. per 100 Cc.
6½ mos.....	9/15/31	36.5	555	79	10.0	4.5	....	...	....	....	....
7 mos.....	10/ 7/31	34.9	538	114	11.4	4.0	23.6	142	4.77	1.54	0.22
8½ mos.....	11/21/31	....	...	84	....	...	....	160	3.66	2.86	0.36
1 yr., 10 mos.....	1/ 7/33	33.1	515	68	9.2	3.6	34.0	...	5.13	3.17	....
2 yrs., 3 mos.....	6/15/33	25.0	485	101	10.0	2.5	35.2	152	4.38	2.59	0.39
2 yrs., 4 mos.....	7/11/33	....	...	...	....	...	52.4	...	....	....	....
3 yrs.....	3/20/34	....	...	...	10.9	5.3	....	...	....	....	....

* Determinations of nonprotein nitrogen, sugar, cholesterol and chlorides were made on whole blood; those of calcium and phosphorus on serum, and those of carbon dioxide and the blood protein fractions on plasma.

A positive reaction was always given to the indirect test, and a negative or faintly positive reaction to the direct test. The intradermal tuberculin test gave a negative reaction with 0.1 and 0.5 mg. The spinal fluid was normal. The Wassermann and the Kahn test of the blood gave negative results. Roentgenograms of the long bones showed moderate osteoporosis. Chemical analyses of the blood, apart from the special studies to be detailed later in the paper, showed normal values during the first stay in the hospital for all the components tested, except the carbon dioxide-combining power, which was low at one time. In January and June 1933, the values for serum phosphorus were low because of the development of active rickets at the time when the patient had begun to gain rapidly. The results of these analyses are given in the table.

The urine was examined repeatedly, and so long as the diet contained milk it almost invariably showed a two plus reaction for albumin, a four plus reaction for sugar, a few granular casts and an occasional red blood cell. Specimens collected early in the morning did not always give a positive reaction for sugar. Sugar was never present in any considerable amount, a twenty-four hour specimen containing only 1 Gm. The fact that the sugar did not ferment with yeast, as dextrose does, made us suspect that we were dealing with another sugar. Dr. G. L. Foster, of

the department of biological chemistry, identified the sugar as galactose. His conclusion was based on evidence obtained in the following tests:

A specimen of the urine was treated with lead acetate to remove interfering substances. The excess lead was removed with hydrogen sulphide, and the specimen was finally decolorized with charcoal.

Reduction: Fifty-four hundredths per cent of sugar (expressed as the equivalent of dextrose) was found by the Shaffer-Hartmann method.

Rotation: A 1 decimeter tube with the green line of the mercury spectrum was used. A dextrorotation of 0.56 degrees was observed. The specific rotation of pure galactose is 96 degrees to the right with the green line of the mercury spectrum. Assuming the sugar to be galactose and using the well known equation for the determination of the percentage of sugar, percentage $= \frac{\text{Observed rotation} \times 100}{\text{Specific rotation} \times \text{length of tube}}$, we have $\frac{0.56 \times 100}{96 \times 1} = 0.58$ per cent, a value which agrees closely with the percentage of sugar as determined by the method of reduction.

Osazone: Osazone was prepared from a clarified specimen of urine, washed with water and alcohol and dried at 110 C. The crystals appeared identical with those known to be galactosazone. They melted at 193 C., and caused no depression of the melting point when mixed with known galactosazone.

Phloroglucin Test: The reaction was brownish red like that given with galactose.

Hydrolysis: A specimen of the urine was acidified to approximately seven-tenths-normal with hydrochloric acid and boiled for one hour. The reducing power increased only slightly, from 0.54 to 0.6 per cent. This result excluded the presence of a disaccharide in larger quantity than a trace.

By the time the sugar had been identified, the infant had been in the hospital nearly five months and had gained only 700 Gm. He had had several mild infections of the respiratory tract. His appetite was always poor, and from time to time he regurgitated a considerable amount of food. There was little change in his appearance, and the liver and spleen were fully as large as on his admission. As a therapeutic experiment, based on the identification of the urinary sugar, the milk in the diet was markedly reduced on Feb. 4, 1932, when he was 11 months old. Within two days the reducing substance had disappeared from the urine. Albumin disappeared from the urine a few days later. In the next month he gained over 500 Gm. On March 4 all the milk was stopped, and the feeding of Sobee,[4] a soy bean substitute for milk, was started. From that time he gained and grew rapidly. At 23 months of age he weighed 14 Kg. (30 pounds and 13 ounces). By that time he was walking well and talking a little. In March 1932 and in January 1933, he was fed 200 cc. of milk as a clinical experiment. On each occasion the reducing substance reappeared in the urine a short time after the milk was taken. Since then he has continued to grow and gain satisfactorily on a milk-free diet. On March 26, 1934, when he was just past 3 years of age, he weighed 17.3 Kg. (38 pounds and 1 ounce).

After he had been on a milk-free diet for several months, it became apparent that the liver and spleen were decreasing in size. At the time of writing, the spleen was barely palpable, and the liver extended only 2 inches below the costal margin in the right mammary line. The edge of the liver was firm. The van den Bergh test of the serum gave a negative reaction. The bones no longer showed osteoporosis. He walked and talked normally for his age and in fact appeared well,

4. Sobee consists of soy bean flour, olive oil, arrowroot starch, dextrimaltose (essentially maltose and dextrin), dicalcium, acid phosphate and sodium chloride.

except for the moderate enlargement of the liver and the inability to manage any considerable amount of lactose or galactose.

In brief, the case is that of a Negro infant who did not gain and develop normally as long as his diet included milk. Furthermore, he excreted galactose and albumin in the urine, and the liver and spleen were enlarged. The patient's rapid improvement and continued progress after the removal of milk from the diet made it practically certain that the primary defect was inability to convert ordinary amounts of absorbed galactose into dextrose. Because the conversion is a function of the liver and because of the findings on physical examination, we postulated the existence of a congenital or an acquired lesion of the liver. It is remarkable, however, that the functions of the liver, other than the one concerned in the conversion of galactose into dextrose, were apparently unaffected. When the demand on this one function was removed, there was an astonishingly rapid return to normal health. As we were unable to understand why the patient's health should have suffered so severely, and as it was inconceivable that the daily loss of a few grams of carbohydrate in the urine could interfere with growth, the patient was readmitted to the hospital for a period of further study.

STUDIES ON CARBOHYDRATES

The levels of the total blood sugar [5] after feeding dextrose, levulose, galactose and lactose (1.75 Gm. per kilogram of body weight) were first determined. The curves for dextrose and levulose were within normal limits. The curves for both galactose and lactose were abnormal in that it took two hours for the level of the total reducing substances of the blood to reach the maximum height and from seven to eight hours to return to the level for fasting (chart 1).

5. At first we determined the total reduction by the Folin-Wu micromethod (Folin, O.: J. Biol. Chem. **77**:421, 1928). This method was used by Dr. H. Alexander in making the determinations shown in chart 1. After this we adopted Gibson's finger-tip method (Gibson, R. B.: Proc. Soc. Exper. Biol. & Med. **27**: 480, 1930) and determined not only the total blood sugar but the fermentable and nonfermentable fractions. This method employs 0.2 cc. of blood and gives about 5 cc. of the tungstate filtrate, 2 cc. of which was used for the determination of the total blood sugar. The amount of galactose in the remaining 2 cc. was measured after removal of the dextrose by fermentation with standard yeast. Somogyi's method (Somogyi, M.: J. Biol. Chem. **75**:33, 1927) was used in the preparation of the yeast suspension. It was found necessary to keep the yeast suspension at room temperature for at least three hours before using it, in order to obtain complete fermentation of the dextrose present. Blood filtrates containing known amounts of dextrose were fermented, after which no reduction in the solution took place. No correction, therefore, was necessary for reducing substances other than dextrose or galactose. When galactose was added to a Folin-Wu filtrate, recovery of the amount varied from 94 to 104 per cent. The term "galactose" is used as referring to the nonfermentable fraction of the blood filtrate.

A similar amount of galactose given to a normal child of the same age resulted in a similar increase of the reducing substances with the maximum height of the curve occurring at the end of one hour. As compared with that of the patient, however, the fall in the level was

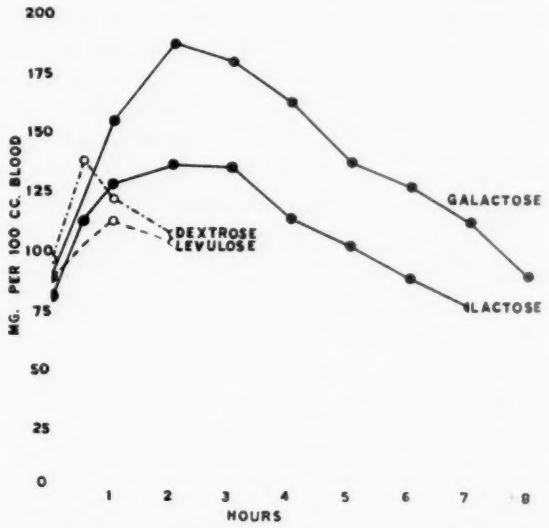

Chart 1.—Values for the blood sugar obtained for the patient after ingestion of 1.75 Gm. per kilogram of body weight of dextrose, levulose, lactose and galactose, respectively.

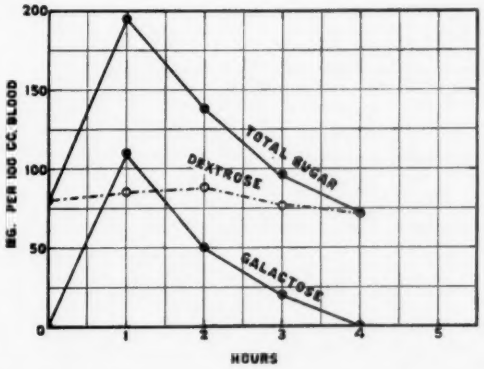

Chart 2.—Values for total blood sugar, galactose and dextrose obtained for a normal infant of the same age as the patient after ingestion of 1.75 Gm. per kilogram of body weight.

more rapid, and the level for fasting was reached by the fourth hour (chart 2). By fractionating the blood sugar it was found that the level of the blood dextrose remained practically unchanged throughout the experiment. The level of the blood galactose, however, rose from zero

to over 100 mg. per hundred cubic centimeters in the first hour and then fell rapidly. At four hours galactose had disappeared from the blood.

A similar galactose tolerance test, with fractionation of the blood hexoses, was performed on the patient. The curve for the total blood sugar was similar to that shown in chart 1. The curve for galactose (nonfermentable fraction) reached its maximum height at the end of two hours, fell rapidly during the third hour, and then declined more slowly. Eight hours after ingestion there was still considerable galactose in the blood. The curve for dextrose fell slightly for two hours and then rose in the third hour, coincidentally with the decline in the curve for galactose (chart 3).

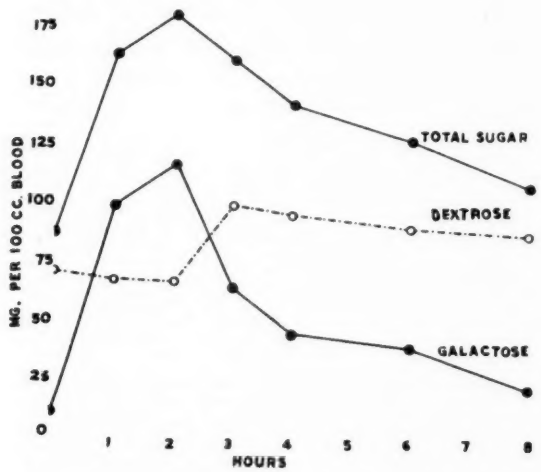

Chart 3.—Values for total blood sugar, dextrose and galactose obtained for the patient after ingestion of 1.75 Gm. of galactose per kilogram of body weight.

In another tolerance test (chart 4) specimens of urine were collected before and at intervals of one-half, one, two, three, four and seven hours after the ingestion of 25 Gm. of galactose. The urine collected during the seven hours of the experiment contained 6.64 Gm. of nonfermentable sugar, calculated as dextrose. No sugar was present in the urine before galactose was ingested. During the first half-hour after the ingestion, 0.2 Gm. of sugar was excreted; during the second half-hour, 0.75 Gm.; during the second hour, nearly 3 Gm.; during the third hour, 1.75 Gm.; during the fourth hour, 0.75 Gm., and during the fifth, sixth and seventh hours, a total of only 0.2 Gm. No attempt was made to determine the threshold, but it is obvious that the excretion of sugar (galactose) began within one-half hour of the ingestion of galactose and

that from that time the amount excreted increased as long as the level of the blood sugar rose and diminished as the level of the blood sugar fell.

At this stage, then, it was shown that the patient was unable to manage galactose normally. He apparently absorbed it normally but was unable to convert it into dextrose or glycogen at the normal rate. This failure resulted in the level of blood galactose reaching its maximum height two hours instead of one hour after ingestion and in the persistence of galactose in the blood long after it would normally have disappeared from the blood. A considerable part of the ingested galactose must have been converted or stored, at least temporarily, for during the eight hours of the experiment only about a quarter (26.5 per cent)

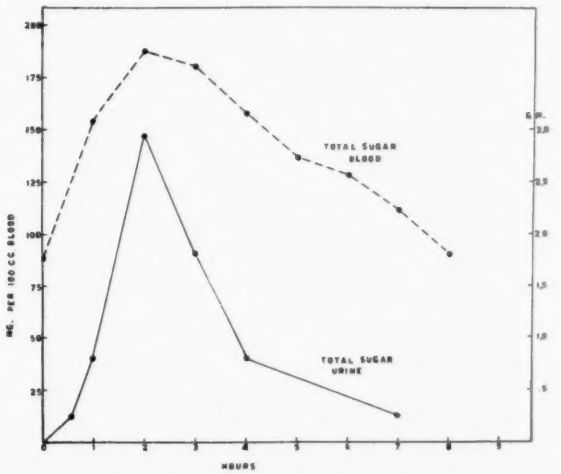

Chart 4.—Values for total blood sugar and sugar in the urine (total amount excreted, 6.64 Gm.) after ingestion of 1.75 Gm. of galactose per kilogram of body weight.

of the quantity ingested was excreted. And yet no explanation of the profound effect on the general health of an apparently mild disturbance was forthcoming.

In order to compare the conditions prevailing when the patient was gaining rapidly with those obtaining during the periods of his failure to gain, the amount of blood sugar was determined at hourly intervals throughout the day—first when the diet contained no milk, and again when to the same diet had been added 200 cc. of milk and 10 Gm. of lactose (a total of about 19 Gm. of lactose), with each meal and an equivalent amount of fat, protein and carbohydrate had been withdrawn (chart 5). A normal curve was obtained when the diet contained no milk, but the curve was distinctly abnormal when the diet contained

milk and lactose. With the latter diet the total level of blood sugar rose after each meal and then fell gradually until after the next meal, when it rose again; but at no time did it rise as high as after a milk-free meal, even though the amount of carbohydrate was the same in each case. The curve for galactose paralleled that for the total blood sugar, but at a lower level. At no time during the day, when milk was fed, was the blood free from galactose. The curve for dextrose

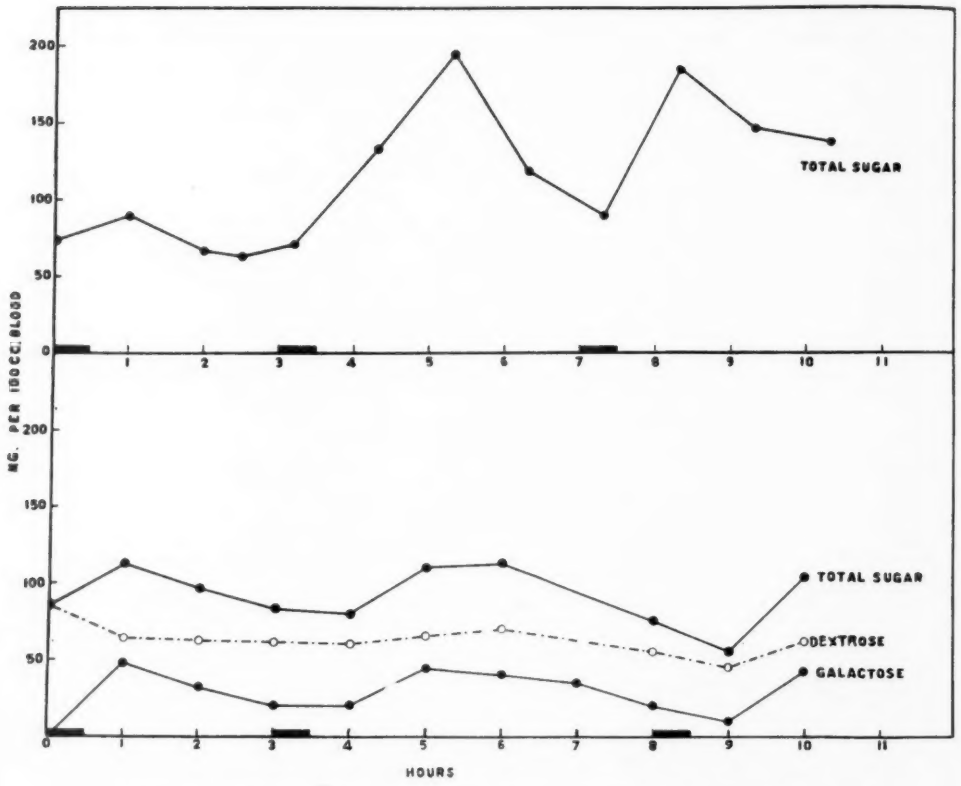

Chart 5.—Hourly values for blood sugar, dextrose and galactose obtained throughout the day. In this chart and in the following charts the upper curve represents the values obtained when the patient received a milk-free diet containing 80 Gm. of carbohydrate in each meal and the period of the meal is indicated by a heavy line along the abscissa. The values represented by the curves in the lower part of the chart are those obtained when the patient received a similar diet except that 200 cc. of milk and 10 Gm. of lactose were substituted in each meal for equivalent amounts of protein, fat and carbohydrate.

differed. It declined to a level of about 60 mg. per hundred cubic centimeters after breakfast at a time when it may have been expected to rise and when the concentrations of total blood sugar and galactose

were increasing, and remained there through the day, in spite of the ingestion and apparent absorption of 80 Gm. of carbohydrate at each meal, only about 9 Gm. of which consisted of galactose. The course of the curve suggested that the bulk of the absorbed dextrose did not pass the liver but was removed from the portal blood and stored in the liver as fast as it appeared. If this was so, the enlargement of the liver may have been due to an enormous storage of glycogen. Furthermore, the continuously low level of blood dextrose may well have been the cause of the patient's inability to gain and of most of the other symptoms.

It is interesting to speculate on the reason that the level of the total blood sugar did not rise as high after meals on the milk-containing as on the milk-free diet. It is generally conceded that the body possesses a mechanism for lowering the amount of blood sugar, which is brought into action when the blood sugar rises beyond a certain level. These curves suggest that it is the height of the level of the total blood sugar and not that of dextrose alone which sets in motion the mechanism for lowering the blood sugar level. They further suggest that in this patient the mechanism for lowering the level of the blood sugar could not act efficiently on galactose and therefore acted excessively on dextrose, thus keeping it at an abnormally low level.

The effect of epinephrine was next determined when the patient was on both the milk-free and the milk-containing diet (chart 6). When 5 minims of a 1 : 1,000 solution of epinephrine was given subcutaneously two hours after breakfast, a characteristic rise in the level of the blood dextrose resulted, whether the blood contained galactose or not. Epinephrine did not, however, influence the level of the blood galactose, which continued to fall slowly as in the preceding experiment. In other words, in this patient epinephrine was able to mobilize dextrose but not galactose. In fact, there was no observable effect on galactose.

The effect of insulin was unexpected (chart 7). When 5 units was given subcutaneously three hours after a breakfast containing no galactose, there was a characteristic fall in the level of blood sugar (that is, of dextrose) from 78 to 31 mg. per hundred cubic centimeters in twenty minutes. At this point the patient showed symptoms of slight shock. After this point and in the course of several hours, the amount of blood sugar gradually rose to the preceding level. When the breakfast contained 200 cc. of milk and 10 Gm. of added lactose, the subcutaneous injection of 5 units of insulin was followed by a rapid rise and a subsequent fall in the amount of the total blood sugar. Fractionation of the blood sugar showed that there was a typical decrease in the amount of blood dextrose from 38 to 13 mg. per hundred cubic centimeters, and at the same time a marked increase in the amount of blood galactose. So great was the increase in the amount of galactose that

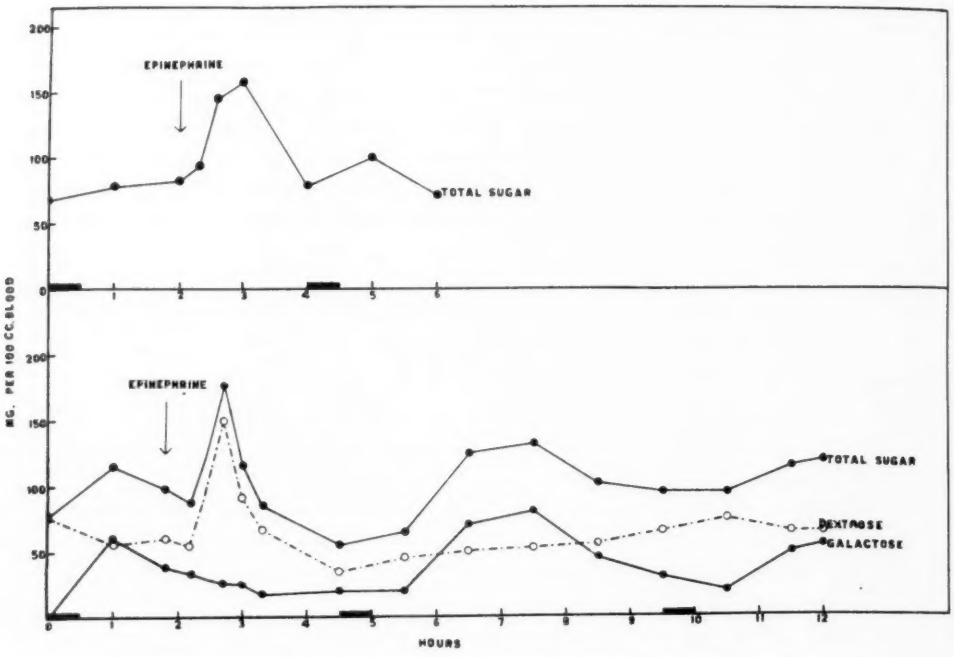

Chart 6.—Effect of 5 minims of a 1: 1,000 solution of epinephrine on the values of total blood sugar, dextrose and galactose.

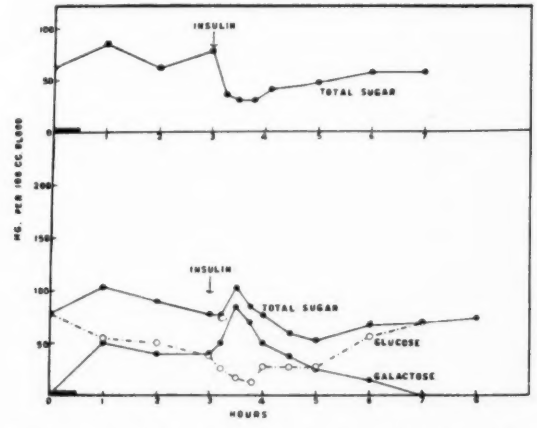

Chart 7.—Effect of 5 units of insulin on the values for the total blood sugar, dextrose and galactose.

the level of total blood sugar rose rather than declined. The patient showed no symptoms of shock at any time, although the concentration of blood dextrose decreased to 13 mg. per hundred cubic centimeters. As he showed distinct symptoms of shock when the level of blood dextrose fell to 31 mg. per hundred cubic centimeters in the absence of galactose in the blood, it seems that the absence of shock when the level of blood dextrose was 13 mg. per hundred cubic centimeters must be attributed to the presence in the blood of a considerable amount of galactose.

The mechanism responsible for the action of insulin in increasing the amount of blood galactose is obscure. We have considered two possible explanations. It is conceivable that insulin may act in such a way as to prevent galactose from leaving the blood and entering the tissues, so that with continued absorption there is an accumulation in the circulation. It is difficult to believe, however, that enough galactose was still being absorbed after three hours to counteract the effect of renal excretion. On the other hand, it is possible to conceive that galactose actually entered either the liver or the tissues but was not converted into dextrose and that in some way insulin forced it back into the circulation. Perhaps the galactose was ejected to make way for a more easily usable sugar. In either case it is clear that insulin acted on both dextrose and galactose. The action is in harmony with the suggestion in an earlier part of the paper that the mechanism for lowering the level of blood sugar acts on a sugar other than dextrose, for insulin is one of the factors known to be concerned in the mechanism.

COMMENT

In both Göppert's patient and our own the outstanding clinical symptom was failure to gain and to grow properly, and the chief findings were enlargement of the liver and spleen and the presence of galactose and albumin in the urine so long as the child received any considerable amount of milk. In both cases withholding the milk brought about a remarkable change in the picture. First galactose and a few days later albumin disappeared from the urine. At the same time the child began to gain and to grow in a normal way. The spleen became smaller, and the liver stopped increasing in size and then became smaller. Thereafter progress was rapid and uneventful. Relief from the stress imposed by a single defective physiologic function changed the whole picture. Why this should be so is difficult to understand.

One is faced with the following questions: What was the primary condition that was responsible for the inability of the patient to manage ordinary amounts of galactose? Was this primary condition responsible for the patient's other symptoms, such as the failure to gain, or

were these symptoms the result of a secondary derangement of the metabolism?

Regarding the first question the evidence is now strong that the liver is the chief, and possibly the only, organ capable of converting galactose into dextrose. This fact suggests that in the cases under consideration there was a lesion of the liver which resulted in marked lowering of the ability to manage galactose. As the lowering of the galactose tolerance was marked in each case, the lesion must have been diffuse, involving many cells of the liver. The size and consistency of the liver suggest cirrhosis, but the marked decrease in size when the patient was placed on a milk-free diet makes it doubtful that the entire enlargement was due to this cause. The cause of the cirrhosis is not clear. Syphilis was ruled out in both cases. In our case the pneumonia at 6 months of age may have been the cause. In Göppert's case the prolonged jaundice suggests the existence of biliary cirrhosis. On the other hand, it is conceivable that a congenital defect may have been the cause.

Even if defective function of the liver is accepted as the basis of disturbance in these cases, the second question remains to be answered. If the other symptoms, such as failure to gain, albuminuria, marked enlargement of the liver, etc., were directly due to the hepatic lesion, one would not expect relief from mere elimination of the demand on the liver to convert galactose into dextrose. On the other hand, if the symptoms were the result of a secondary metabolic change, such as might ensue from the continuous presence of galactose in the blood or from a continuously low level of blood dextrose, relieving the liver of the stress would be expected to effect general improvement. This we believe is the probable explanation.

Some of the findings may be examined in greater detail. So long as the patients were fed a considerable amount of milk, the liver continued to increase in size. When milk (lactose) was withheld, the liver stopped enlarging and then decreased in size. If the original enlargement had been due to uncomplicated cirrhosis, it would hardly have disappeared so promptly. There are two other possible explanations for the enlargement of the liver, i. e., excessive storage of either fat or glycogen. While positive proof is not forthcoming, we are inclined to believe that the enlargement which later disappeared was due to excessive storage of glycogen. The explanation is in accord with the continuously low level of blood dextrose when the patient was on a milk-containing diet. The course of events, as we have conceived it, was as follows: Milk in the diet resulted in galactose reaching the general circulation; the circulating galactose maintained the total blood sugar at a level high enough to stimulate the mechanism for lowering the blood sugar, and this mechanism, unable to act satisfactorily on the galactose, acted excessively on the dextrose and caused the storage of abnormally large

amounts in the liver. When milk was withdrawn from the diet, galactose disappeared from the blood; the level of the blood dextrose again rose, and gradually the excess of stored glycogen was discharged from the liver. The explanation depends on the validity of an earlier suggestion that it is the height of the level of the total blood sugar and not that of dextrose alone which sets in motion the mechanism for lowering the amount of blood sugar.

Why did these children gain so slowly while receiving milk, and why did they gain so rapidly when milk was withheld? It could not have been due to the loss of sugar and albumin in the urine, because these losses were insignificant. Perhaps the failure to gain was due to an insufficient intake of food, for it was difficult to make our patient take enough food until milk was withdrawn from the diet. Göppert did not mention this point. Another explanation may be that the tissues were relatively starved as a result of the continuously low amounts of blood dextrose. To us this is the probable explanation, because it accords with the rest of the picture.

Why did these patients show albuminuria as long as they excreted galactose, and why did albuminuria disappear shortly after galactosuria ceased? Other abnormal phenomena were present as well, including a positive van den Bergh reaction, anemia and osteoporosis of the bones, and these also disappeared when milk was eliminated from the diet. The fact is strongly suggested that the conditions were not primary but secondary, dependent in some way on the continuous presence of galactose in the circulation. Two explanations present themselves: first, that galactose was diffused into all the tissues and in some way interfered with the normal activity of the cells and, second, that the continuously low level of blood dextrose caused relative starvation and imperfect function of the cells. The situation may be analogous to that in cases of diabetes mellitus occurring in children; these patients often show albuminuria when the diabetic condition is first recognized and lose it when they become sugar-free as the result of treatment.

SUMMARY

The report deals with the case of an infant who did not gain normally so long as the diet contained milk and who also showed marked enlargement of the liver, slight enlargement of the spleen and superficial lymph nodes, a positive reaction to the van den Bergh test, secondary anemia, osteoporosis of the bones and albumin and sugar in the urine. The sugar in the urine was determined to be galactose.

Removal of milk from the diet resulted in the disappearance of sugar and albumin from the urine, decrease in the size of the liver and spleen, disappearance of the positive van den Bergh reaction and

improvement in the blood and in the appearance of the bones, as well as a rapid gain in weight.

The curves for blood sugar after the ingestion of dextrose and levulose were within normal limits, but after that of lactose and galactose, the curves were abnormal in course.

When the diet contained no milk, the blood sugar curve throughout the entire day was within normal limits. When each meal contained 200 cc. of milk and 10 Gm. of added lactose, the curve for the blood sugar was abnormal in that the fluctuations were narrow and were due almost entirely to changes in the level of blood galactose. The level of blood dextrose remained low throughout the day.

Subcutaneous injection of epinephrine resulted in a normal response, the level of the blood dextrose rising sharply whether there was galactose in the blood or not.

Insulin caused a fall in the level of the blood dextrose, whether there was galactose in the blood or not. On the milk-containing diet the level of the total sugar rose after the injection of insulin, the rise being due to a marked increase in the amount of blood galactose.

The findings are discussed in the light of the present knowledge of sugar metabolism. It is suggested that the primary trouble in our case was a lesion or functional disturbance of the liver that lowered the ability of this organ to convert galactose into glycogen without seriously impairing the other functions of the liver, and that the derangement of the other tissues was the result of relative starvation, due to the continuously low level of blood dextrose.

RESPIRATORY EXCHANGE IN CHILDREN FOLLOWING ADMINISTRATION OF VARIOUS CARBOHYDRATES

RELATION TO THE CURVES FOR BLOOD SUGAR

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A survey of the literature shows that little investigation on the effect of various carbohydrates on the respiratory quotient in children has been made and that there are few observations on the blood sugar curves obtained with these sugars.

The object of the work reported in this paper was to find the relative influences of dextrose, fructose, sucrose, lactose, galactose and dextrimaltose on the respiratory quotient and on the curves for blood sugar and to determine the relation, if any, between them.

The observations were carried out on a girl aged 11 years, who was under treatment for chronic syphilitic vaginitis. The culture obtained from material from the vagina was positive, but there was no discharge. She was afebrile, ambulatory and apparently healthy.

METHOD OF STUDY

For several days preceding the first test the patient was placed on a diet of known weight, which was maintained throughout the observations. Approximately 30 calories per pound (453.59 Gm.) of body weight were allowed, with 1 Gm. of protein, 3 Gm. of carbohydrate and 1.5 Gm. of fat per pound of body weight, giving a ratio of 0.5. This diet furnished just sufficient calories to maintain weight and to supply energy for the usual activities.

The subject was trained to relax as far as possible and to breathe regularly and evenly during the test. Her cooperation was excellent, and the respiratory quotients may be considered reliable from this point of view.

The basal metabolic rate and the respiratory quotient were obtained in the postprandial state twelve hours after the taking of food. The subject, E. G., arrived at the laboratory at 4:50 a. m. The first of a number of specimens of urine taken every four hours was obtained. She then rested quietly on a couch in the metabolism room for twenty minutes before the determination of the basal metabolic rate.

From the Department of Pediatrics and Infectious Diseases, University of Michigan, Mead Johnson Infant Feeding Research Fund.

After the basal metabolic rate and respiratory quotient had been determined, 1.75 Gm. of carbohydrate per kilogram of body weight, dissolved in 200 cc. of water, was ingested, and tests were made at intervals of one-half, one, two, three and four hours.

A 100 liter Tissot spirometer equipped with a rubber mouthpiece was used. Two washings were made before the beginning of the test, and the duration of the test in each experiment was six minutes. Readings on the spirometer were checked. Analysis of the expired air was duplicated with the Haldane-Henderson apparatus for gas analysis. The results agreed to within 0.03 per cent of an atmosphere; otherwise the analysis was repeated.

Allowance was made for the metabolism of protein by determination of the nitrogen content of the four hour sample of urine collected on the morning of the test, and the nonprotein respiratory quotient was calculated from this.

Difco sugars (chemically pure) were used in all observations.

OBSERVATIONS ON MONOSACCHARIDES

Dextrose.—As the result of the ingestion of 48 Gm. of dextrose, the respiratory quotient increased gradually in the first three periods, reaching its peak of 0.92 at the end of the third hour and then falling to about its basal point in the fourth hour. The greatest increase in the production of heat occurred one-half hour after the ingestion of the dextrose. The maximum respiratory quotient occurred two hours after the peak of the blood sugar curve. The level of the blood sugar determined simultaneously with the appearance of the maximum respiratory quotient was near that obtained during fasting (tables 1 and 2, chart 1).

Galactose.—Galactose became available promptly. One-half hour after its ingestion the basal respiratory quotient rose from 0.78 to 0.92. The maximum respiratory quotient, 0.93, was obtained at the end of the third hour, while a low quotient of 0.69 was noted at the end of the fourth hour. The maximum production of heat was manifest at the end of the second hour. As with dextrose, there was no relation between the height of the curve for blood sugar and the maximum respiratory quotient, as the highest quotient occurred one hour later than the highest peak in the blood sugar curve. In a preliminary report by Lichty and Law [1] the respiratory quotient in one of the subjects showed little response to the ingestion of galactose. We were unable to interpret this observation and wished therefore to verify it. The response obtained with galactose in the present observation is more in keeping with the results of earlier work done on adults and is what one would expect.

Fructose.—With fructose, as with galactose, there was a prompt, although not as great, increase in the respiratory quotient in the first half hour. The availability of this carbohydrate, as indicated by the respiratory quotient, was more delayed than that of galactose. The maximum respiratory quotient was reached at the end of one hour, after which there was no additional increase. The greatest production of heat occurred at the end of the first hour. With fructose there was a close approximation of the appearance of the peak of the blood sugar curve and of the maximum respiratory quotient, the maximum respiratory quotient occurring at the height of the blood sugar curve at the end of the first hour.

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1. Lichty, D. E., and Law, J. L.: Effect of Various Carbohydrates on the Nonprotein Respiratory Quotient, Am. J. Dis. Child. **48**:224 (July) 1934.

TABLE 1.—*Effect of Ingestion of Various Carbohydrates on the Level of the Blood Sugar* *

Time	Monosaccharides			Disaccharides		
	Dextrose, Mg. per 100 Cc.	Fructose, Mg. per 100 Cc.	Galactose, Mg. per 100 Cc.	Sucrose, Mg. per 100 Cc.	Lactose, Mg. per 100 Cc.	Dextrimaltose, Mg. per 100 Cc.
Fasting						
6 a. m.	105	100	88	96	98	98
After ingestion						
30 minutes	150	105	125	132	163	147
60 minutes	159	125	149	116	109	154
120 minutes	121	115	167	106	107	122
180 minutes	113	112	98	98	94	105
240 minutes	96	94	91	95	96	89

* Forty-eight Gm., or 1.75 Gm. per kilogram of body weight, of the sugar was given in each test.

TABLE 2.—*Effect on Respiratory Quotient and Production of Heat of Ingestion of 48 Gm. of Various Carbohydrates* *

Monosaccharide	Dextrose				Fructose				Galactose			
Date	3/2/34				3/10/34				3/6/27			
Weight of subject	26.8 Kg.				27 Kg.				27 Kg.			
	Nonprotein Respiratory Quotient	Total Calories per Hour	Percentage of Increase in Heat Production	Metabolic Rate, Percentage	Nonprotein Respiratory Quotient	Total Calories per Hour	Percentage of Increase in Heat Production	Metabolic Rate, Percentage	Nonprotein Respiratory Quotient	Total Calories per Hour	Percentage of Increase in Heat Production	Metabolic Rate, Percentage
Basal value	0.75	46.86	..	+4.0	0.74	49.0	....	+ 8.5	0.76	44.5	..	+ 1.3
Time after ingestion												
30 min.	0.84	49.23	5	+9.3	0.87	55.1	12.5	+22.2	0.92	45.0	0	— 0.23
60 min.	0.87	47.98	2	+6.5	0.913	56.6	16.0	+27.2	0.84	46.2	4	+ 2.5
120 min.	0.87	48.20	3	+6.9	0.89	53.0	8.2	+15.5	0.88	52.7	19	+16.9
180 min.	0.92	43.30	−8	−3.8	0.86	46.0	−6.0	+ 2.9	0.93	49.1	10	+ 8.9
240 min.	0.81	47.00	0	+4.5	0.77	50.8	4.0	+12.8	0.69	49.9	12	+ 2.1

Disaccharide	Sucrose				Lactose				Dextrimaltose			
Date	3/11/34				3/4/34				3/12/34			
Weight of subject	27 Kg.				26.8 Kg.				27.2 Kg.			
	Nonprotein Respiratory Quotient	Total Calories per Hour	Percentage of Increase in Heat Production	Metabolic Rate, Percentage	Nonprotein Respiratory Quotient	Total Calories per Hour	Percentage of Increase in Heat Production	Metabolic Rate, Percentage	Nonprotein Respiratory Quotient	Total Calories per Hour	Percentage of Increase in Heat Production	Metabolic Rate, Percentage
Basal value	0.83	40.9	..	— 9.2	0.75	46.1	..	+ 3.34	0.75	44.7	..	— 0.7
Time after ingestion												
30 min.	1.02	51.4	26	+14.2	0.87	52.5	14	+16.6	0.88	52.0	16	+15.6
60 min.	0.85	53.9	32	+19.6	0.87	49.4	7	+ 9.7	0.90	51.1	14	+13.5
120 min.	0.83	49.2	20	+ 9.3	0.92	49.1	7	+ 8.9	0.82	51.4	15	+14.1
180 min.	0.88	48.5	19	+ 7.6	0.85	36.5	0	+ 3.3	0.89	49.5	10	+ 9.87
240 min.	0.79	43.7	7	— 3.0	0.76	46.1	0	+ 2.4	0.74	46.5	4	+ 3.2

* The average percentage of increase in heat production over the basal rate for the one-half, one, two and three hour periods for the various sugars were as follows: sucrose, 24; dextrimaltose, 14; fructose, 8; galactose, 8; lactose, 7, and dextrose, 0.5.

OBSERVATIONS ON DISACCHARIDES

Sucrose.—Sucrose produced a prompt elevation of the respiratory quotient, which increased from a basal value of 0.83 to one of 1.02 at the end of one-half hour. The quotient obtained at the end of one-half hour was the highest reached during any period of observation after the administration of a sugar. At the end of four

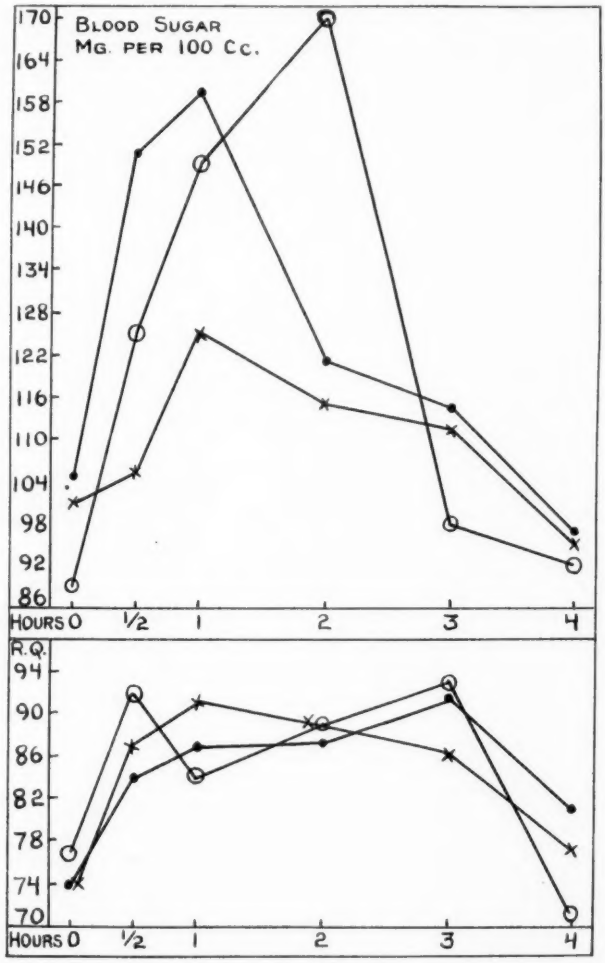

Chart 1.—Graphs showing the values for blood dextrose, fructose and galactose and for the respiratory quotient, obtained at intervals after ingestion of 48 Gm. of each monosaccharide. In this chart the value for dextrose is represented by a curve of lines and dots; that for fructose, by lines and crosses, and that for galactose, by lines and circles.

hours the respiratory quotient had fallen to slightly below the basal level. The maximum production of heat occurred at the end of the first hour. Both the maximum respiratory quotient and the peak of the blood sugar curve took place in one-half hour (tables 1 and 2, chart 2).

Lactose.—After the administration of 48 Gm. of lactose the increase in the respiratory quotient was slower than after that of sucrose and was less marked. A definite increase occurred in one-half hour, but the appearance of the maximum respiratory quotient (0.92) was delayed until the end of the second hour. At the end of four hours the quotient had returned to its basal level. The maximum

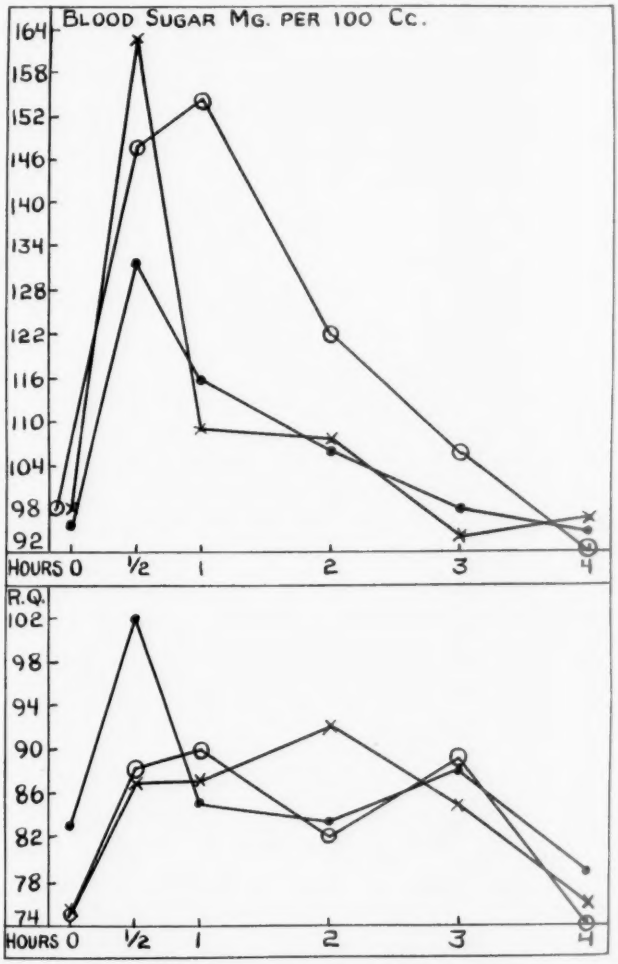

Chart 2.—Graphs showing the values for blood sucrose, lactose and dextrimaltose and for the respiratory quotient, obtained at intervals after ingestion of 48 Gm. of each disaccharide. In this chart the value of sucrose is represented by a curve of lines and dots; that for lactose, by lines and crosses, and that for dextrimaltose, by lines and circles.

production of heat took place in one-half hour, while the maximum respiratory quotient occurred one and one-half hours after the peak of the blood sugar curve.

Dextrimaltose.—The results obtained with dextrimaltose were somewhat similar to those with dextrose, a moderate increase in the respiratory quotient occurring

in the first one-half hour, followed by a fairly well sustained curve. The maximum respiratory quotient was obtained at the end of one and of three hours, and the quotient returned to its basal level at the end of four hours. The maximum heat production, as in the case of dextrose, was reached in one-half hour. The peak of the blood sugar curve and that of the respiratory quotient coincided at the end of the first hour.

Curves for Blood Sugar.—The investigation of the influence of the ingestion of 48 Gm. of various carbohydrates on the course of the blood sugar curve (Folin-Wu method) showed that the ingestion of lactose produced in one-half hour a sharp rise to a peak of 163 mg. per hundred cubic centimeters, that the curve for dextrose rose more slowly and reached a lower peak of 159 mg. per hundred cubic centimeters at the end of one hour and that, though the curve for galactose rose more slowly than that for lactose or dextrose, the peak of 167 mg. per hundred cubic centimeters reached at the end of two hours was higher than that with any of the other carbohydrates. The elevation with dextrimaltose was less marked, reaching a peak of 154 mg. per hundred cubic centimeters at the end of one hour. Sucrose and fructose produced less effect on the sugar content of the blood than any of the other carbohydrates (table 2; charts 1 and 2).

SUMMARY OF FINDINGS

The availability of the various carbohydrates, as expressed by the rapidity of the increase in the respiratory quotient in the one-half hour period after ingestion, occurred according to the following order: sucrose, galactose, fructose, dextrimaltose, lactose and dextrose.

The greatest increase in the respiratory quotient obtained in any period with any carbohydrate was that with sucrose, which was the only carbohydrate with which the quotient reached 1. This was obtained in one-half hour. Galactose gave the next highest quotient (0.93) obtained in any period, and this value was reached at the end of the third hour. The highest respiratory quotient obtained with dextrose was 0.92 in three hours; with lactose, 0.92 in two hours, and with fructose, 0.91 in one hour. With dextrimaltose, which gave the smallest increase, the maximum quotient was reached in one and in three hours.

The average value for the basal respiratory quotient for all carbohydrates was 0.76. The greatest increase over the basal quotient obtained with any carbohydrate was that with sucrose with which a difference of 0.19 in the respiratory quotient occurred. With fructose, galactose, dextrose and lactose the greatest increase over the basal respiratory quotient was 0.17. The smallest difference in the quotients, 0.15, was that obtained with dextrimaltose.

The rate of increase in the production of heat of the carbohydrates investigated was as follows: Sucrose gave an increase of 32 per cent over the basal value in one hour; fructose, of 16 per cent in one hour; galactose, of 19 per cent at the end of two hours; dextrimaltose, of 16 per cent in one-half hour, and lactose, of 14 per cent in one-half hour, while with dextrose the rate of increase over the basal production of heat usually occurred from one-half to one hour after the administra- of heat was only 5 per cent in one-half hour. The maximum production

tion of the carbohydrate. The only parallelism between the maximum production of heat and the highest respiratory quotient lay in the fact that the greatest increase in heat production occurred from one-half to two and one-half hours before the respiratory quotient reached its peak, except in the case of fructose and sucrose. The average percentage of increase in heat production for the four periods of one-half, one, two and three hours was as follows: sucrose, 24 per cent; dextrimaltose, 14 per cent; galactose, 8 per cent; fructose, 7 per cent; lactose, 7 per cent, and dextrose, 0.5 per cent. The increase in heat production demonstrated by our subject was greater than the increases shown by those in the experiments reported by Lichty and Law.[1]

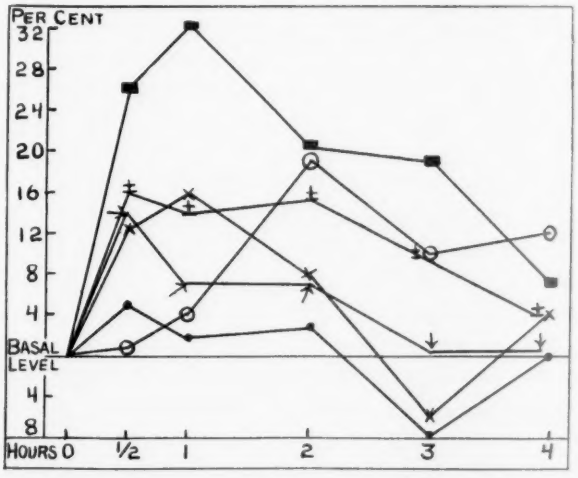

Chart 3.—Effect of various carbohydrates on the percentage of increase of heat production over the basal level. In this chart the value for dextrose is represented by lines and dots; that for fructose, by lines and crosses; that for galactose, by lines and circles; that for sucrose, by lines and squares; that for lactose, by lines and arrows, and that for dextrimaltose, by lines and the plus and minus signs.

It will be seen from charts 1 and 2 that there is no specific relation between the height of the blood sugar curve and the respiratory quotient. The maximum respiratory quotient occurred one hour after the height of the blood sugar curve with galactose, one and one-half hours later with lactose and two hours later with dextrose. With sucrose, fructose and dextrimaltose the maximum respiratory quotient and the peak of the blood sugar curve were simultaneous—with sucrose in one-half hour, with fructose in one hour and with dextrimaltose in one hour. There was only a moderate increase in the copper-reducing value of the blood with fructose and sucrose.

A closer parallelism between the appearance of the peak of the blood sugar curve and that of the height of the increase in heat production is apparent. With galactose, fructose, lactose and dextrimaltose the peaks were simultaneous, and with dextrose and sucrose there was a close approximation (table 3).

COMMENT

The respiratory quotient represents the sum of a series of physiologic reactions and not merely the combustion of food at a particular time involving certain chemical changes. It has been shown frequently in adults that the ingestion of various carbohydrates causes characteristic and prompt changes in the respiratory quotient, yet even with the carbohydrates which may be rapidly utilized the respiratory quotient probably

TABLE 3.—*Interval After Ingestion of Various Carbohydrates of Appearance of Maximal Respiratory Quotient, Peak of Blood Sugar Curve and Greatest Production of Heat*

Carbohydrate	Time of Highest Respiratory Quotient, Hours	Time of Peak of Blood Sugar, Hours	Time of Greatest Heat Production, Hours
Dextrose	3	1	½
Fructose	1	1	1
Galactose	3	2	2
Sucrose	½	½	1
Lactose	2	½	½
Dextrimaltose	1 to 3	1	½ to 1

represents more than mere combustion. Being cognizant of the limitations of the indirect method of calorimetry in short experiments, we wished to determine in children the effect on the respiratory quotient of various carbohydrates. All the results are strictly comparable, as they were obtained under identical conditions, and for the day on which an observation was conducted they may be assumed to represent a correct picture of the combustion of the carbohydrate used. The results are somewhat different from those obtained in adults and in animals.

Lusk [2] found that in dogs, with the ingestion of 50 Gm. of various carbohydrates, the highest average respiratory quotient and the greatest increase in metabolism occurred with the various sugars in the following order: fructose, sucrose, dextrose, galactose and lactose. In our observations the greatest average increase in metabolism occurred with sucrose; then came that with dextrimaltose, with galactose, with fructose and, lastly, with dextrose.

Fructose failed to give as great an increase in the respiratory quotient as has been recorded in most observations made elsewhere (Lusk,[2]

2. Lusk, G.: J. Biol. Chem. **20**:555, 1915; The Science of Nutrition, Philadelphia, W. B. Saunders Company, 1928; J. Biol. Chem. **13**:27, 1912.

Cathcart and Markowitz,[3] Deuel and his co-workers,[4] Benedict and Carpenter [5] and Higgins [6]). The production of heat with this sugar was lower than that recorded for Lusk's dogs, though comparable with the average increase of 9 per cent in heat production over the basal value obtained for adults by Deuel.

In our observations galactose did not give as high a respiratory quotient as was found by other workers. The average increase of 8 per cent in the production of heat is identical with that obtained by Deuel. The respiratory quotient of 0.69 obtained in the fourth hour in the case of galactose is low but compatible with some quotients recorded in the literature.

The blood sugar curves for fructose, dextrose and galactose correspond to those obtained by Bodansky [7] in dogs given 3 Gm. per kilogram of body weight or approximately from 30 to 40 Gm. of carbohydrate. Ingestion of fructose resulted in a curve with a low peak; dextrose gave a curve with a moderate rise, and galactose a curve with an abrupt, high peak.

The results of Folin and Berglund's [8] work with dextrose, fructose, galactose and lactose are comparable to ours in the case of fructose and dextrose but not in the case of galactose and lactose, with which the curves were much lower than were found in our experiments.

Foster [9] found that the ingestion of 100 Gm. of galactose produced a fairly rapid increase in blood sugar and a curve with a high peak. These results were similar to those we obtained.

Cathcart's and Markowitz's [3] investigation of the values of blood sugar obtained in adults using 50 Gm. of the various carbohydrates showed that the curves for dextrose and fructose were comparable to ours but that the values obtained with galactose and lactose were much lower.

CONCLUSIONS

From the recorded observations made on one child aged 11 years, after the administration of 48 Gm. of various carbohydrates, there seems to be a difference in the reaction of the various sugars on the respiratory exchange.

The rapidity of the increase in the respiratory quotient produced by the various sugars in the one-half hour period occurred according to

3. Cathcart, E. P., and Markowitz, J.: J. Physiol. **63**:21, 1927.

4. Deuel, H. J., Jr.: J. Biol. Chem. **75**:367, 1927. Deuel, H. J., and others: J. Biol. Chem. **67**:xxiii, 1926. Deuel, H. J., Jr.; Gulick, M., and Butts, J. S.: J. Biol. Chem. **92**:xxiii, 1931.

5. Benedict, F. G., and Carpenter, T. M.: Publ. 261, Carnegie Institution of Washington, 1918, p. 171.

6. Higgins, H. L.: Am. J. Physiol. **41**:258, 1916.

7. Bodansky, M.: J. Biol. Chem. **56**:387, 1923.

8. Folin, O., and Berglund, H.: J. Biol. Chem. **51**:213, 1922.

9. Foster, G. L.: J. Biol. Chem. **55**:291 and 303, 1923.

the following order: sucrose, galactose, fructose, dextrimaltose, lactose and dextrose.

The greatest increase in the respiratory quotient during any period with any carbohydrate was obtained with sucrose; galactose gave the next highest quotient, followed by dextrose, lactose, fructose and dextrimaltose.

The increase over the basal respiratory quotient was greatest with sucrose, the difference in the respiratory quotients being 0.19. With each of the other carbohydrates there was a difference of 0.17, except with dextrimaltose, with which the difference between the basal and the highest respiratory quotient was 0.15.

The average percentage of increase in the production of heat over the basal rate during the first four periods of observation was as follows: sucrose, 24 per cent; dextrimaltose, 14 per cent; fructose, 8 per cent; galactose, 8 per cent; lactose, 7 per cent, and dextrose, 0.5 per cent.

For the various carbohydrates the approximation of the time of the greatest increase in the production of heat over the basal rate and that of the peak of the blood sugar curve was close.

No real parallelism could be plotted between the peak of the respiratory quotient and that of the blood sugar curve, and the difference in response of the respiratory quotient after the ingestion of the various carbohydrates seemed to bear no relation to the differences in the rate and the degree of absorption, as shown by the blood sugar curves.

Our results are comparable to those in much of the work done on adults, except those concerned with fructose and dextrose.

CHOICE OF FORMULAS MADE BY THREE INFANTS THROUGHOUT THE NURSING PERIOD

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During the course of an experimental study of self-selection of diet by newly weaned infants [1] carried on for several years in a nursery organized for this purpose the question of whether a new-born child could successfully exercise a choice of formula and regulate the quantities taken at feedings naturally suggested itself. This report outlines the experiment (also carried on in this nursery) designed to investigate that question and presents the results obtained during 1930 and 1931 with three breast-fed infants taken from lying-in hospitals at the ages of 10, 8 and 7 days, respectively, and subjected continuously to the experiment for periods of from seven and one-half to eight months.

Since there were obvious difficulties involved in presenting to such young infants a large number of formulas for choice at each feeding, it was decided to use for the experiment only four formulas which would be more or less representative of the types of feeding commonly in use and to offer all four at each feeding throughout the nursing period. The four formulas were as follows:

1. A proprietary "reconstructed" milk (Similac) in which for cow's milk fat there has been substituted a mixture of homogenized fats the physiochemical properties of which more nearly approach those of the fat of woman's milk and in which some readjustment of the salts in the direction of the salt content of woman's milk has been made and sufficient lactose added to make the total approximately that of woman's milk. Reliquefied according to the manufacturer's direction, its percentage composition and caloric value are stated to be: fat, 3.4 per cent; carbohydrate, 6.8 per cent; protein, 1.5 per cent; salts, 0.4 per cent, and calories per ounce, 19.

2. Fermented lactic acid milk, made daily from whole pasteurized milk to which 5 per cent of Blue Label Karo corn syrup was added. Its percentage composition and caloric value are approximately: fat, 3.5

1. Davis, C. M.: Self Selection of Diet by Newly Weaned Infants, Am. J. Dis. Child. **36**:651 (Oct.) 1928.

per cent; carbohydrates, 8 per cent; protein, 3.5 per cent; salts, 0.75 per cent, and calories per ounce, 23.

3. A simple milk dilution formula made as follows:

Whole milk, boiled ten minutes	20.0 ounces
Water	10.0 ounces
Lactose	1.5 ounces

The percentage composition and caloric value are: fat, 2.33 per cent; carbohydrate, 8 per cent; protein, 2.33 per cent; salts, 0.5 per cent, and calories per ounce, 19.1.

4. An orange juice, egg yolk, sugar, milk and water formula (J. Hess) made as follows:

Whole milk, boiled ten minutes	20 ounces
Egg yolks	1
Orange juice	2 ounces
Water	8 ounces
Cane sugar	1⅓ ounces

The approximate percentage composition and caloric value are: fat, 3 per cent; carbohydrate, 8 per cent; protein, 2.45 per cent; salts, 1.785 per cent, and calories per ounce, 21.4.

No change in the "strength" of any formula was made at any time regardless of the age of the infants.

Four bottles of the same make and size, marked, 1, 2, 3 and 4 to indicate the formulas, were offered at each feeding according to a schedule so arranged that a formula offered first at one feeding would have second, third and fourth place at successive feedings, and so on, thus equalizing the influence of greater hunger at the beginning of feedings. The nipples were of the same brand, size and shape throughout the experiment, and each was tested before feeding to see that it delivered well. During a period of eighteen days midway in the experimental period of the first infant the nipples were numbered, 1, 2, 3 and 4 and alternated on the bottles according to a fixed schedule in order to make sure that a favorite nipple was not a factor in choice. No evidence was found that one nipple was preferred above others.

During feedings the bottles were kept warm by a small water bath, and the infant was held on the nurse's lap and allowed to nurse as long as he wished from the first bottle. When he stopped sucking or if he did not suck, the second bottle was offered, and so on, all four bottles being offered at each feeding. A bottle emptied during the feeding was promptly refilled to insure that the infant had all that he wished of that formula, but no effort was made to get the infant to take more than he wished, the quantities of the feedings being left

wholly to him. Intervals of feeding were at first every three hours during the day and whenever the infant waked at night. These intervals were lengthened from time to time as the infant showed a tendency to sleep over the feeding time or for several days in succession showed little interest in one feeding during the day, the desire being to conform the schedule as closely as possible to the satisfaction and comfort of the infant. Thus the number of feedings in twenty-four hours declined

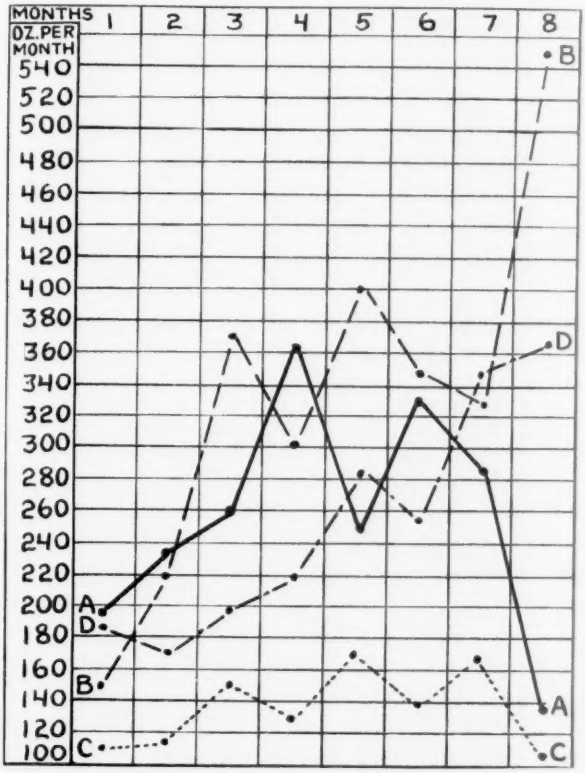

Fig. 1.—Quantities of each formula taken in successive months by Rosemary L. In this and the following charts *A* indicates Similac; *B*, lactic milk and Karo corn syrup; *C*, milk dilution; *D*, egg yolk, orange juice and milk (Hess).

from a maximum of nine (with one infant for one day only) in the first week to four and occasionally three in the last (eighth) month.

To make available ample quantities of antiscorbutic vitamin without compelling the infant to take the orange juice, egg yolk and milk formula (number 4), undiluted orange juice was offered twice daily between feedings to be taken in any amount wished. The reliquefied proprietary milk (number 1), according to the manufacturers' statement, contains 7 drops (0.4 cc.) of cod liver oil per liter. In addition to this,

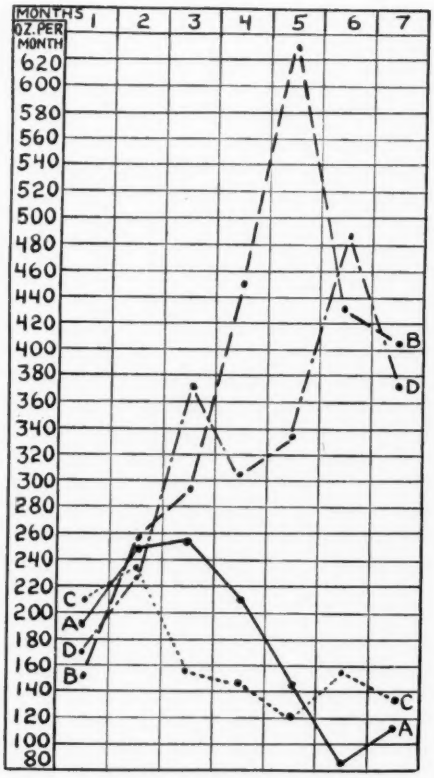

Fig. 2.—Quantities of each formula taken in successive months by Shirley S.

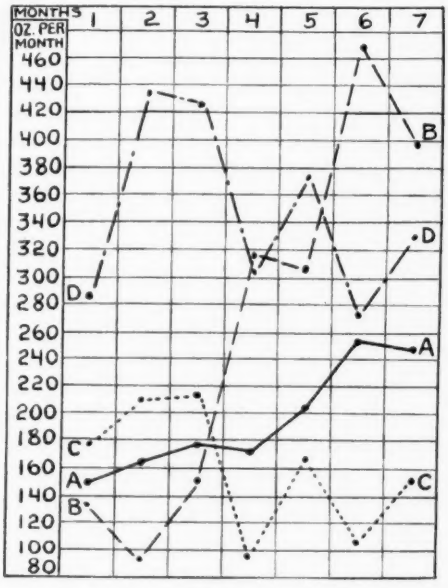

Fig. 3.—Quantities of each formula taken in successive months by Robert H.

cod liver oil was given to the first infant for two periods of twenty-one and sixteen days, respectively, during the first three months, being discontinued at the end of each of the periods because of her evident dislike of it. Cod liver oil was not administered to the other two infants, nor did any of the three receive viosterol, ultraviolet irradiation or sun-baths. Dietary supplements, such as the cereals and vegetables commonly added to the diet at 5 or 6 months of age, were omitted.

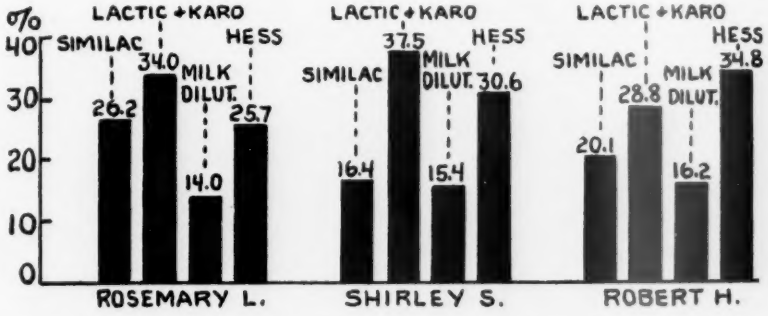

Fig. 4.—Percentage of each formula in the total quantity taken by each infant during the entire nursing period.

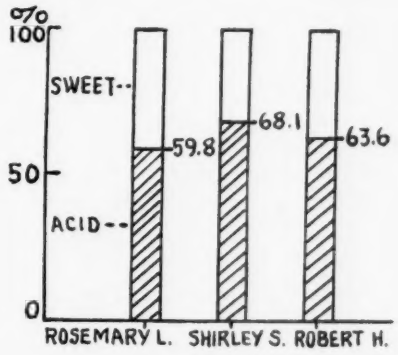

Fig. 5.—Percentages of acid and sweet milks in the total amount taken by each infant during the entire nursing period.

The respective quantities of the four formulas taken by the infants, the range in size and frequency of feedings, the calories consumed per month and the monthly weights of the infants are shown in the accompanying figures and tables, which are self-explanatory.

That differences in taste were appreciated early in the first week was unmistakably evidenced by the behavior of the infants. Lactic acid milk often caused unhappy grimaces and sometimes a distinct shudder on its first entrance into the mouth. Often after a few eager sucks from the first bottle the nipple would be pushed out by the tongue and what

TABLE 1.—*Number of Daily Feedings Taken by Rosemary L. in Successive Months and Their Minimum, Maximum and Average Size*

Month	Number of Days	Number of Feedings per Day	Minimum Ounces at Any Feeding	Maximum Ounces at Any Feeding	Average Quantity per Feeding, Ounces	Total Number of Feedings in Month
1 (Jan.)	31	9 to 7	0.50	5.75	2.76	232
2	28	8 to 6	0.50	8.75	3.83	197
3	31	6 to 5	1.00	11.50	6.14	160
4	30	6 to 4	2.50	10.50	6.70	150
5	31	5 to 4	1.00	15.00	8.06	136
6	30	4	3.50	14.50	8.99	120
7	31	4	1.75	15.50	9.09	120
8	31	4	2.25	18.50	9.50	120

TABLE 2.—*Number of Daily Feedings Taken by Shirley S. in Successive Months and Their Minimum, Maximum and Average Size*

Month	Number of Days	Number of Feedings per Day	Minimum Ounces at Any Feeding	Maximum Ounces at Any Feeding	Average Quantity per Feeding, Ounces	Total Number of Feedings in Month
1 (Aug.)	31	8 to 6	0.75	6.75	3.20	226
2	30	8 to 5	0.75	9.00	4.83	201
3	31	7 to 5	1.00	11.00	6.16	174
4	30	6 to 5	1.50	11.00	7.31	151
5	31	5	1.50	15.00	7.94	155
6	31	5 to 4	3.00	15.00	8.72	133
7	28	4 to 3	2.50	15.75	10.52	98
8	17	3	6.00	18.00	12.55	51

TABLE 3.—*Number of Daily Feedings Taken by Robert H. in Successive Months and Their Minimum, Maximum and Average Size*

Month	Number of Days	Number of Feedings per Day	Minimum Ounces at Any Feeding	Maximum Ounces at Any Feeding	Average Quantity per Feeding, Ounces	Total Number of Feedings in Month
1 (April)	31	8 to 5	1.00	6.00	3.19	233
2	30	7 to 6	2.75	8.50	4.81	187
3	31	6 to 5	0.00	9.50	5.51	174
4	30	5 to 4	1.00	10.00	5.95	149
5	31	5	0.00	13.50	6.75	155
6	31	5	2.50	12.00	7.12	155
7	30	5 to 4	4.50	12.50	8.33	136
8	13	4	6.00	13.00	9.41	52

TABLE 4.—*Average Size of Feedings (in Ounces) Taken in Successive Months by the Three Infants*

Month	Rosemary L.	Shirley S.	Robert H.	Average
1	2.76	3.20	3.19	3.05
2	3.83	4.83	4.81	4.46
3	6.14	6.16	5.51	5.94
4	6.70	7.31	5.95	6.59
5	8.06	7.94	6.75	7.65
6	8.99	8.72	7.12	8.24
7	9.09	10.52	8.33	9.31
8	9.50	12.55	9.41	10.15

TABLE 5.—*Minimum, Maximum and Average Daily Quantity (in Ounces) Taken by Rosemary L. in Successive Months*

Month	Number of Days	Minimum Daily Quantity	Maximum Daily Quantity	Average Daily Quantity
1	31	12.50	27.75	20.600
2	28	18.00	39.75	26.800
3	31	25.75	39.00	31.485
4	30	28.50	44.25	33.525
5	31	23.50	41.75	35.600
6	30	25.75	43.75	35.940
7	31	15.50	44.75	36.380
8	31	23.25	50.50	37.700

TABLE 6.—*Minimum, Maximum and Daily Quantity (in Ounces) Taken by Shirley S. in Successive Months*

Month	Number of Days	Minimum Daily Quantity	Maximum Daily Quantity	Average Daily Quantity
1	31	14.25	30.50	23.30
2	30	26.00	39.75	32.39
3	31	27.25	41.25	34.57
4	30	30.00	40.75	36.80
5	31	33.00	46.75	39.69
6	31	29.25	46.75	37.45
7	28	31.75	43.25	36.83
8	17	31.25	45.25	37.65

TABLE 7.—*Minimum, Maximum and Average Daily Quantity (in Ounces) Taken by Robert H. in Successive Months*

Month	Number of Days	Minimum Daily Quantity	Maximum Daily Quantity	Average Daily Quantity
1	31	16.75	32.75	22.96
2	30	25.75	34.00	29.97
3	31	24.25	34.50	30.90
4	30	24.50	37.50	29.60
5	31	27.00	40.50	33.80
6	31	29.00	42.75	35.62
7	30	29.75	44.00	37.77
8	13	33.50	39.75	37.65

TABLE 8.—*Average Daily Quantities (in Ounces) Taken in Successive Months by the Three Infants*

Month	Rosemary L.	Shirley S.	Robert H.	Average
1	20.60	23.30	23.00	22.30
2	26.80	32.40	30.00	29.70
3	31.50	34.60	30.90	32.30
4	33.50	36.80	29.60	33.30
5	35.60	39.70	33.80	36.40
6	35.90	37.45	35.60	36.30
7	36.40	36.80	37.80	36.90
8	37.70	37.65	37.65	37.66

was in the mouth allowed to run out, after which the infant took the next bottle eagerly. As the infants grew older a bottle might be refused without tasting, probably from a perception of the distinctive and familiar odor of its contents. But in general the keener hunger at the beginning of a feeding resulted in the taking of at least a small amount of the first formula offered.

TABLE 9.—*Average Calories per Kilogram of Weight per Day*

Month	Rosemary L. January	Shirley S. August	Robert H. March
1	114.20	151.21	153.20
2	122.30	151.76	145.90
3	118.00	133.20	127.50
4	115.65	122.00	108.30
5	105.90	113.90	113.70
6	96.50	97.70	108.60
7	93.70	90.00	109.20
8	93.00	87.50	104.60

TABLE 10.—*Amount of Orange Juice (in Ounces) Taken by Each Infant During the Entire Period*

Name	Amount Taken as Such	Amount in Hess Formula	Total Ounces	Average Ounces per Day
Rosemary L.	283.75	134.78	468.53	1.70
Shirley S.	428.00	162.10	590.10	2.58
Robert H.	104.50	168.50	273.00	1.25

TABLE 11.—*Number of Egg Yolks (in Hess Formula) Taken by Each Infant*

Name	Number of Yolks
Rosemary L.	67.60
Shirley S.	81.66
Robert H.	84.26

TABLE 12.—*Cod Liver Oil (in Drachms) Taken by Each Infant During Entire Period*

Name	Administered as Such	Amount Incorporated in Similac	Total Drachms
Rosemary L.	69	7.20	76.20
Shirley S.	0	4.51	4.51
Robert H.	0	4.25	4.25

The infants were wholly free from digestive troubles, such as diarrhea, vomiting, constipation and colic, and they slept soundly, seldom cried and exhibited the vigorous yet serene and contented behavior that is characteristic of the adequately fed and well cared for breast-fed infant. R. L., at the age of 6 weeks, contracted from her night attendant a streptococcic infection (of the upper respiratory

tract) which resulted in bilateral suppurative otitis media, with drainage for four weeks. This was not accompanied by any digestive disturbance or interruption of steady gain in weight. S. S. had one mild cold and R. H. no illness of any kind.

Their nutritional condition appeared to be excellent in every way. Their turgor, muscular development and tone were all that could be desired; their hair was abundant, soft, glossy and fine and grew rapidly. Monthly roentgenograms of their bones for evidence of rickets gave negative results with one exception: The report on S. S. at the age of 5 months was "possibly early slight rickets." The next month, however, the report was "normal; no evidence of rickets," as were subsequent reports.

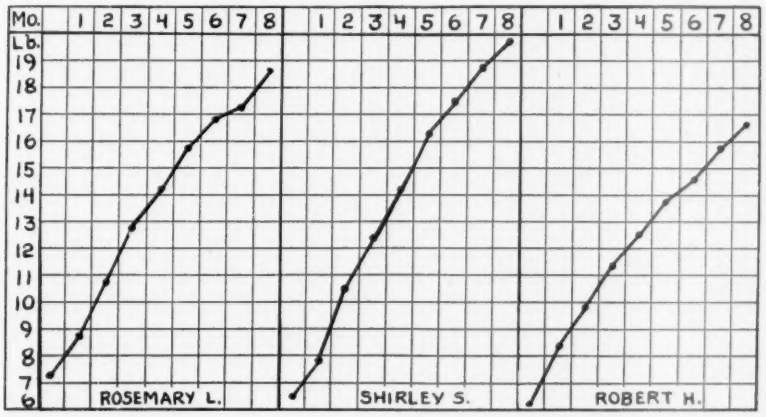

Fig. 6.—Weight charts of Rosemary L., Shirley S. and Robert H., respectively.

COMMENT AND CONCLUSIONS

In view of the fact that healthy vigorous infants have been reared on each of the four formulas and that all are in general well liked by infants, it is not surprising that the preferences shown were moderate in degree, a result to which the necessity of offering bottles successively instead of simultaneously also doubtless contributed.

That all three infants took relatively much less lactic acid milk during the first two months of life than later corroborates the findings of those pediatricians who have reported that this milk is not as readily taken by new-born infants as by older infants. It would be interesting to know why less was taken of the milk dilution formula than of any other. An outstanding difference in its composition from that of all the others is that its fat content is the only one which falls below the 3 per cent that seems to be the base line for this element in the milk of all species.

The most striking feature of their performance, however, is the wide variation in the quantities taken at a feeding. The maximum quantity taken at single feedings in every month seems large, especially in the first three months, for which the figures are: first month, from 5.75 to 6.75 ounces; second month, from 8.5 to 9 ounces; third month, from 9.5 to 11.5 ounces. But with the minimum feedings relatively small—on some occasions little more than a taste—the averages are not out of line with current practice. This pattern of eating behavior, i. e., occasional "stuffing" and meals of widely varying quantities is, of course, the natural one not only of mammalian young in general but also of the breast-fed baby. Furthermore, it is not merely an infantile pattern but one that continues to a greater or less degree throughout life. Artificially fed infants appear to be the only large group on whom identical quantities for successive meals are meticulously imposed, and one cannot but wonder whether the comfort of these infants who exercised choice not only of formulas but of quantities and their complete freedom from digestive discomforts and symptoms of any sort were not due rather to the following of this natural eating pattern than to the combinations made by their choices of formulas.

SUMMARY

An experiment in which three infants were allowed their choice of four formulas from the first week throughout the nursing period is reported, with figures and tables showing the performance of each infant and comments on the results.

695 Prospect Avenue.

BLOOD CELLS IN HEALTHY YOUNG INFANTS

II. A COMPARISON OF ROUTINE AND SPECIAL TECHNICS IN THE DIFFERENTIATION OF LEUKOCYTES

ALFRED H. WASHBURN, M.D.
DENVER

In the first paper [1] of this series on the blood cells in early life the rationale of the study was described in some detail. It might be stated briefly as an attempt to define the variations in the number and types of blood cells which are consistent with health in infancy as distinguished from those which indicate the presence of disease. Following the first contribution, which dealt with the fluctuations in the total white cell blood count, chief emphasis has been placed on a study of the differential leukocyte count. When this phase of the investigation was started about 300 differential counts had been done already by routine methods,[1] using a fixed smear on a cover-slip with Wright's stain. Before starting a more thorough and painstaking study of the different types of white cells and their fluctuations in healthy babies it seemed wise to check the results obtained with the routine method against results obtained by more specialized technics. The data arising from these comparisons seem sufficiently interesting to warrant this separate report. The complete analysis of over 600 differential counts, together with a final tabulation of over 900 total leukocyte counts, follows as the third paper of the series.

COMPARISON OF COUNTS ON FRESH DROP PREPARATIONS AND ON FIXED SMEARS

The first problem undertaken was a comparison of the differential counts on supravitally stained fresh drop preparations and fixed smears stained with Wright's stain. These were made, so far as possible, from successive drops of blood flowing freely from the infant's heel. The fresh drops were stained with neutral red and janus green B. The fixed smears were made on cover-slips and stained with Wright's stain.

From the Child Research Council and the University of Colorado School of Medicine.

1. Washburn, A. H.: Blood Cells in Healthy Young Infants: I. The Leukocytic Picture During the First Three Months with Special Reference to Hourly and Daily Variations, Am. J. Dis. Child. **47**:993 (May) 1934.

Reports by Forkner,[2] Sabin and her co-workers,[3] Smith,[4] Benjamin and Ward,[5] Rogers [6] and others have suggested that one might obtain a more correct picture of the distribution of the different types of cells with the supravital technic. The simplest safe method of checking this suggestion seemed to be by comparing: (1) counts done on the fixed smear with those done at the same time on the same baby by means of the vitally stained fresh drop, (2) counts done on this same series of fixed smears with a second series of counts done on the same smears and (3) the average of these two series of counts done on the fixed smears with the series of counts done on the fresh drop preparations. It was felt that such a series of comparisons would show whether there was any constant difference in the distribution of cell types in well made fixed smears and in fresh drops of living blood cells. The second series of differential counts would then serve as a control on the extent and consistency of these differences as well as demonstrate the approximate reliability of the average count by routine methods, counting from 200 to 300 white cells.

Six healthy babies in the nursery of the Florence Crittenton Home were utilized for this study. They were observed carefully from birth to the time of leaving the institution, which varied from the third to the sixth month. One hundred differential counts were done for each of the three series, making a total of 300 counts for complete comparison. The technic of the method of counting on fixed smears has been described in the first paper of the series.[1] The technic followed for the supravital staining was similar to that described by Forkner,[2] 200 cells being counted.

The leukocytes were divided into the following groups: polymorphonuclears, immature polymorphonuclears, myelocytes, eosinophils, basophils, large lymphocytes, small lymphocytes, monocytes, blast cells and unclassified cells. The grouping of cells for this part of the study was: polymorphonuclears, lymphocytes (large and small) bone marrow cells (all the granulocytes), monocytes and immature cells.

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2. Forkner, C. E.: Studies on the Living Blood Cells of the Newborn, Bull. Johns Hopkins Hosp. **45**:75 (Aug.) 1929.

3. Sabin, F. R.; Cunningham, R. S.; Doan, C. A., and Kindwall, J. A.: The Normal Rhythm of the White Blood Cells, Bull. Johns Hopkins Hosp. **37**:14 (July) 1925.

4. Smith, C. H.: The Differential White Count in Infancy: Comparison by Supravital and Fixed Smear Methods, Am. J. Dis. Child. **40**:505 (Sept.) 1930.

5. Benjamin, B., and Ward, S. M.: Leukocytic Response to Measles, Am. J. Dis. Child. **44**:921 (Nov.) 1932.

6. Rogers, P. M.: A Study of the Blood Monocytes in Children with Tuberculosis, New England J. Med. **198**:740 (May 24) 1928.

The results of these comparisons are shown in figures 1 to 5. Each chart depicts the size and distribution of the difference in percentage for some one cell type as it was found in comparing: (1) the specimens stained supravitally and those stained with Wright's stain; (2) the first and second series of differential counts on the fixed smears prepared with Wright's stain, and (3) the average of these two series with the counts on the vitally stained fresh drops. For the sake of simplicity the deviation is given directly in terms of the actual percentage of the total number of white blood cells. In each chart the plus sign (+) indicates a greater percentage found in the first series of fixed smears prepared with Wright's stain, while the minus sign (—) indicates a smaller percentage in the first series of counts on the fixed smears. A brief consideration of each of these five figures will help to answer the question concerning the distribution of cells in the fixed smear as compared with that in the fresh drop.

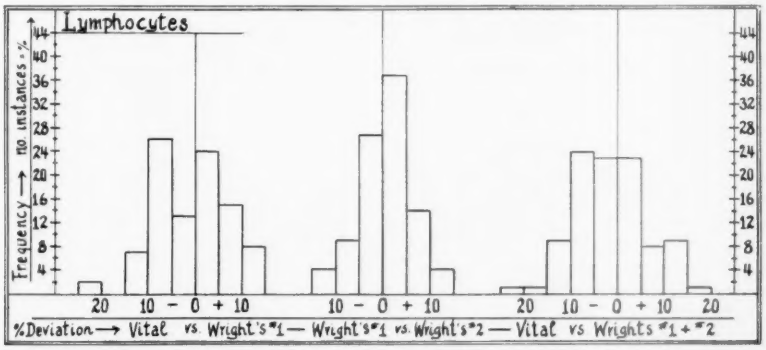

Fig. 1.—Distribution of differences in the percentage of lymphocytes in three series of 100 differential counts, with supravital staining of fresh drops and Wright's stain on fixed smears. In this and the succeeding charts the same three series of 100 differential counts are referred to; the plus sign indicates a greater percentage in the first series of fixed smears with Wright's stain and the minus sign, a smaller percentage.

In figure 1 is shown the variation in the percentage of lymphocytes in each of the three series of counts. When one compares the counts on the fresh drops and those on the fixed smears one finds just as many instances (forty-eight) in which there were more lymphocytes in the fresh drop as those in which there were more lymphocytes in the fixed smear (forty-seven). In the central figure of the chart it will be noted that while the spread of the deviation in percentage is less, the difference between the numbers of plus and minus instances is greater in this comparison of the two series of fixed smears prepared with Wright's stain (— 40 and + 55). In view of the obviously large errors involved, this difference is probably not significant, but it may serve to

emphasize the similarity in the distribution when the fresh drop and fixed smear are compared. Averaging the counts of the two series prepared with Wright's stain tends to smooth out the distribution of the differences, but when compared with the count of the vitally stained fresh drops the picture is one of more lymphocytes in the fresh drop than in the fixed smear. This serves chiefly to emphasize the size of the possible error in the average differential white blood cell count.

Figure 2 shows the difference in the percentage of polymorphonuclears in each of the three counts. As with the lymphocyte the spread is considerably less when one compares the two series of counts on the fixed smear, though there were five instances even in this case in which the deviation was greater than 10 per cent. In both the comparisons between the vitally stained preparations and those stained with Wright's

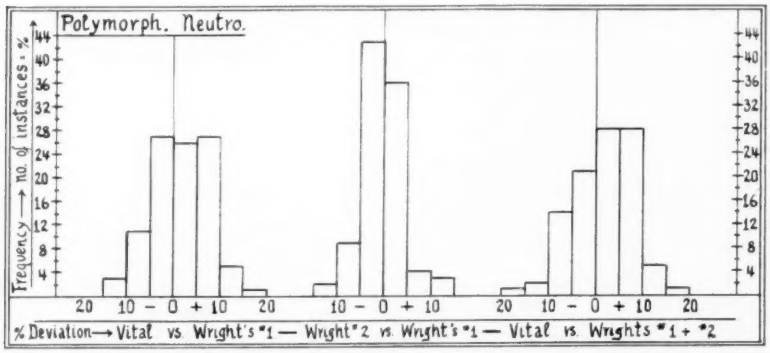

Fig. 2.—Distribution of differences in the percentage of polymorphonuclears.

stain there were more instances in which the count of polymorphonuclears was higher in the fixed smear than in the fresh drop. These differences amounted to + 59 and — 41 in the one comparison and + 62 as against 38 in the other. Whether these are significant variations or not they suggest that the polymorphonuclears are at least not increased in numbers in the fresh drop.

When one groups together (fig. 3) all the granulocytes one sees much the same picture as for the neutrophils alone. Only two differences are worth noting. In comparing the two series of counts on smears prepared with Wright's stain the distribution is somewhat smoother, with forty-nine instances on the plus side and forty-six on the minus side. Also, in the two comparisons of counts on the fresh drops with those on the fixed smears there are fewer instances in which the percentage of granulocytes was higher in the fixed smears. Thus, the figures are + 55 and — 41 for one comparison and + 59 and — 41 for the other.

Figure 4, showing the deviations in the monocyte counts, is of interest because of the great difficulty in classifying all the members of this group by any one method. Some are readily recognized with any of a variety of staining technics, while a few are always open to question even in vitally stained preparations. The left-hand figure of the chart shows that there were more instances in which the percentage of monocytes was higher in the vitally stained fresh drop than in the fixed smear with Wright's stain. On comparing the counts of the two series of smears prepared with Wright's stain one finds ten instances in which the percentages were the same but fifty-three in which the percentage was higher in the second series of counts, which was made several months after the first. Perhaps personal judgment at any one time plays a greater part in the classification of such a

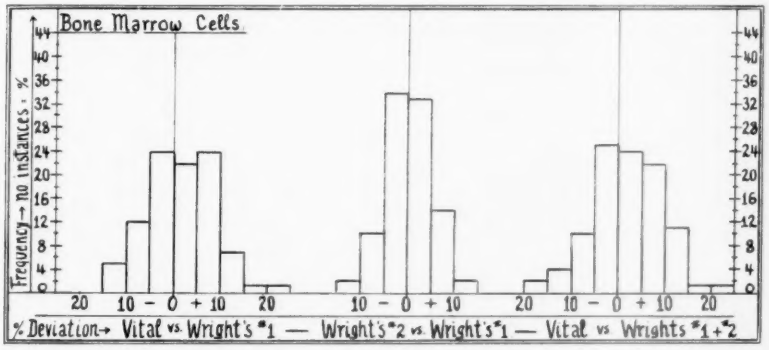

Fig. 3.—Distribution of differences in the percentage of all the granulocytes.

heterogeneous group as the monocytes than in the proper recognition of lymphocytes or neutrophils.

In figure 5 the deviation in percentage of all the immature cells is shown. Interestingly enough the figures in this group represent the most even distribution shown for any of the cell groups in these comparative estimates. Possibly this is dependent on the fact that only cells which were definitely immature were so classified. This point will be elaborated further in the discussion of the Schilling and similar classifications, later in the paper.

Comment.—It is apparent that there is no constant or marked tendency shown for any one cell type to appear in greater numbers in the fresh drop, vitally stained, than in the fixed smear with Wright's stain or vice versa. Such slight tendencies as are noted are toward an increase in the polymorphonuclears and a decrease in the lymphocytes in the fixed smear. This finding is directly contrary to the reports in the

literature which have already been mentioned.[7] If both preparations are properly made and counts are made with painstaking care there would seem to be no good reason for supposing that the distribution of the cells would be markedly different. The charts seem to lend support to this thesis, although they might be criticized because of the great degree of variation noted even between the percentages in the two series of differential counts on the same fixed smears. Some comfort has been gained from the fact that the distribution of the deviation in percentage is fairly even on either side of the zero-line. All the work, from the cleaning of the cover-slips to the final analyzing and charting of the results, was done by one person. Each smear was counted without any knowledge as to what the other differential counts had shown for that baby at that time. The technic in general has been as good as that in the average clinical laboratory. Taking all these

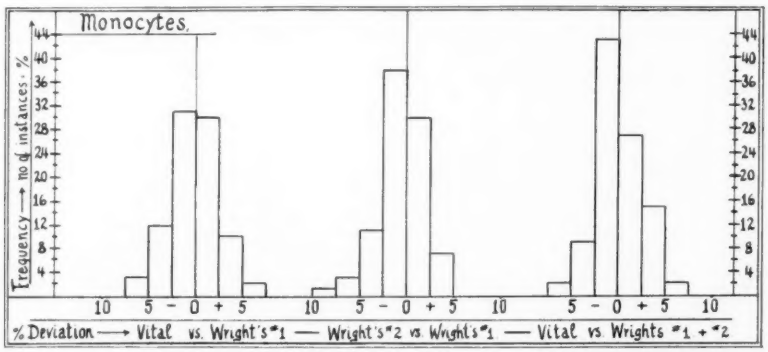

Fig. 4.—Distribution of differences in the percentage of the monocytes.

factors into consideration, it would seem safer to face frankly the fact that there is a fairly large possible error in the differential white blood cell count by any method. With this in mind, the checking of the differential counts on fresh drop preparations and fixed smears would seem to be as close as could be expected.

Although the so-called supravital technic is of undoubted value in the study of blood cells, there are a number of reasons for skepticism as to whether it should be advised for routine use. In any but the most experienced hands there is as much variation in the staining as in a fixed smear. There is a definite time factor leading to haste in the count if an adequate number of cells is to be counted, and haste in making a differential count on such a preparation always leads to inaccuracies. So experienced a worker with vital staining as Dr. Sabin

7. Forkner.[2] Sabin, Cunningham, Doan and Kindwall.[3] Smith.[4] Benjamin and Ward.[5] Rogers.[6]

has pointed out this possible error.[3] The lymphocytes are easily overlooked, especially when haste is required, and this may lead to an apparent increase in the number of granulocytes in the vitally stained preparation. In counting the same preparations, both rapidly and slowly, I have noted an invariable decrease in the percentage of lymphocytes in the rapid counts. Fragmentation of leukocytes may occur in either fresh drop preparations or fixed smears, being particularly difficult to avoid with preparations of the blood of small infants. In my experience with babies there are usually more lymphocytes broken than any other type of cell. When the fragmentation is not complete these are more likely to be classifiable with Wright's stain (a combined peroxidase and Wright's stain is useful in studying the blood in this condition). If one adds to these arguments the fact that the technic of preparing the slides for vital staining, of making the fresh drop preparation and of doing

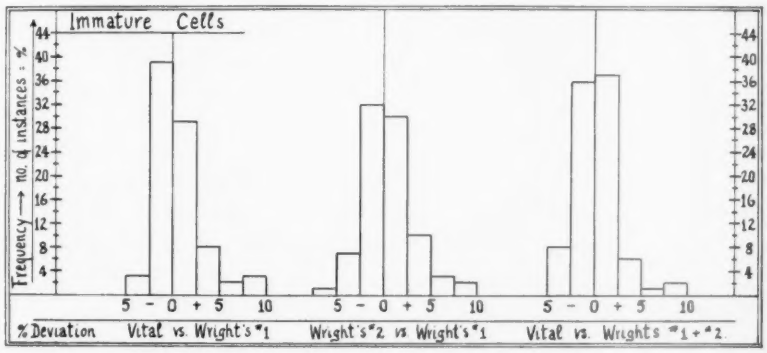

Fig. 5.—Distribution of differences in the percentage of all the immature cells.

the count are all more difficult, one feels justified in taking the attitude that the fixed smear stained with Wright's stain is the method of choice for routine work.

The classification of the monocyte is difficult by any technic. At least in the blood of the infant monocytes vary from a cell which resembles closely certain of the large lymphocytes to one which is similar to a juvenile form of the neutrophil (fig. 6). The charts give evidence of the uncertainty of classification with the fixed smear and Wright's stain. Typical forms are easily classified by any method, while atypical forms are often difficult to classify even in the vitally stained fresh drop, which probably represents the method of choice for their identification. There are two other means of assuring their proper recognition which have not received adequate notice in the literature. The first is a study of their particular type of ameboid motion in fresh drop preparations. This is most characteristically seen in unstained preparations,

in which they show almost continual undulations of the limiting membrane of the cell, thrusting out here and there but actually moving more slowly than the neutrophil. The second aid in their classification consists in using a combined peroxidase and Wright's stain on the fixed smear. The distribution of the oxidase granules in the majority of the cells is very characteristic (fig. 6). I have used such a stain [8] with considerable advantage in the smears of the blood from infants whose blood seemed to contain an unusually large number of atypical mononuclear forms.

CLASSIFICATION OF IMMATURE CELLS

It seems probable that immature cells of every group of leukocytes appear in the circulating blood of the young infant. In this study no attempt was made to separate from the whole group of lymphocytes those large forms which might well be considered as immature cells, nor have immature-looking monocytes been differentiated from the whole group of large mononuclears. Furthermore, the occasional very immature cell with a deep blue cytoplasm and a large round nucleus (fig. 6) has been classed merely as a blast cell, without attempting to state whether it was a lymphoblast or a myeloblast. Considering the inadequacy of the present knowledge, such a simplification of the classification seems justifiable for routine work. This leaves as the only real problem the proper classification of the neutrophil group.

Many attempts have been made to formulate definite criteria for the degree of maturity of this myelogenous group of cells. Arneth's method of counting the number of lobes of the nucleus of the neutrophil has had many proponents, some of whom have published modifications and simplifications of the original Arneth index. Arneth's original classification was very complex, involving five main divisions with from fifteen to twenty subdivisions. By tabulating the cells in such a way that those with the least segmentation or lobulation of the nucleus were on the left and those with the greatest degree of segmentation were on the right, one can refer to a "shift to the left" as indicating an increase in immature forms, while a "shift to the right" indicates a decrease in immature forms or a relative increase in mature forms. In general most classifications of this kind are based on the assumption that the maturity of the cell is directly proportional to the degree of segmentation of the nucleus. After studying the blood of infants and children for ten years I find that assumption very difficult to accept. In addition to the nuclear shape one should consider the chromatin make-up of the nucleus, the size of the whole cell and the appearance of the cytoplasm with special reference to its granular content. Without going

8. Washburn, A. H.: A Combined Peroxidase and Wright's Stain for Use in Routine Blood Smears, J. Lab. & Clin. Med. **14**:246 (Dec.) 1928.

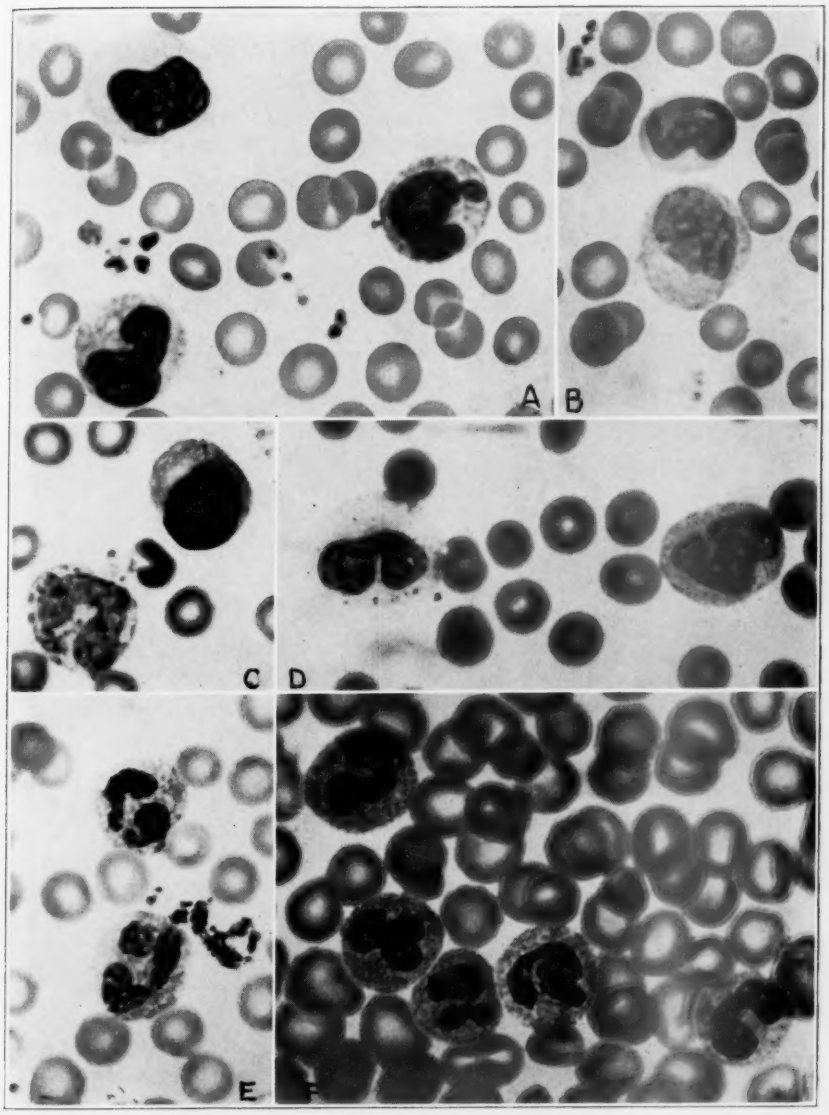

Fig. 6.—Characteristic leukocytes from infants' blood: *A*, variation in monocytes; *B*, contrast between a monocyte and a lymphocyte; *C*, characteristic clumping of oxidase granules in a monocyte and a blast cell above it; *D*, monocytes (peroxidase and Wright's stain); *E*, a mature neutrophil contrasted with a slightly immature form, and, *F*, varying degrees of maturity in neutrophils and a juvenile form in the lower right-hand corner. *A*, *B*, *E* and *F* were stained with Wright's stain.

any further into this debatable question of safe criteria for estimating the maturity of the neutrophil, about which so much has been written while so little is actually known, there are other arguments against the routine use of even a simplified Arneth classification.

It is too cumbersome a method of classifying cells to be useful for routine clinical laboratory work. In his study of the polymorphonuclear count Medlar [9] made a comment which seems particularly apropos. He said: "Any laboratory method which can be of routine value should be reduced to the minimum of work consistent with giving as much information as possible." The added amount of information gained by counting the nuclear lobes is in no way commensurate with the added

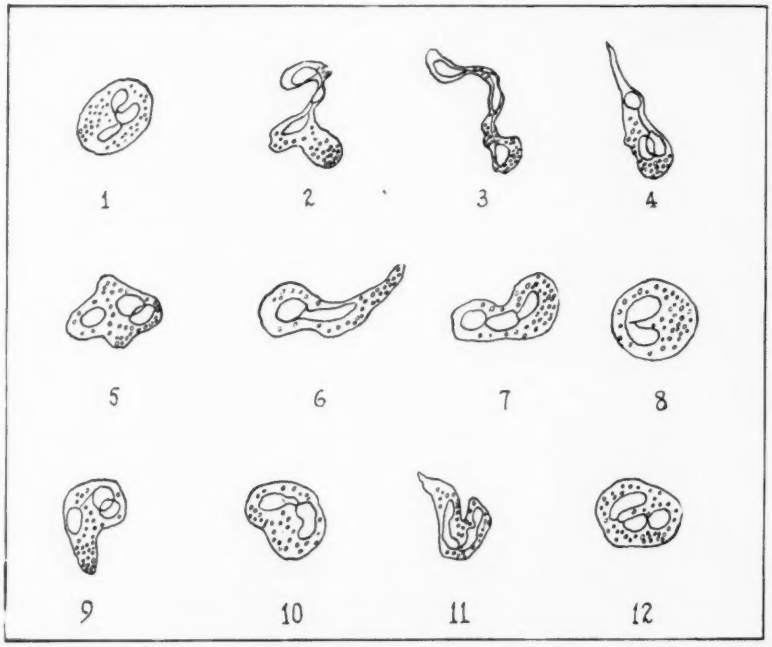

Fig. 7.—Phases in the ameboid wanderings of a three-lobed polymorphonuclear neutrophil. The shape of the nucleus and the outline of the cell were traced accurately from the original sketches, which were selected from a larger series covering a two hour study of this cell.

amount of time and energy spent. A second argument deserves more attention than it has received in the literature. Not only is the task of determining the number of lobes in every polymorphonuclear time-consuming, but accurate accomplishment by the average laboratory worker is well nigh impossible. These cells are not in life standard-

9. Medlar, E. M.: A Critical Study of the Polynuclear Count as Advocated by Schilling, J. Lab. & Clin. Med. **17**:169 (Nov.) 1931.

ized in shape, as they are apt to be pictured in textbooks. Rather, they present nuclei of almost every conceivable configuration. They are, after all, three-dimensional structures which may be caught in the fixed smear so that they are seen from many angles. Furthermore, a study of the living cell in a fresh drop preparation reveals that the nuclear shape may change in a given cell during various stages of its ameboid wanderings (fig. 7). The overlapping of lobes may give a four-lobe polymorphonuclear the superficial appearance of a two-lobe or three-lobe cell. Thus, the method is not only cumbersome but also subject to errors which will make the resultant figures far from accurate. In the infant there is further reason for caution in attaching significance to such a classification. This is dependent on the wide range of variation in the number of neutrophils with from one to five lobes either in one baby from time to time or in different babies. Table 1 shows the variation and the average figures for these cells in 40 counts on three individual infants between the first and twentieth weeks after birth.

TABLE 1.—*Classification of the Neutrophils by Lobes in Forty Differential Counts on Three Infants from One to Twenty Weeks of Age*

	Number of Lobes					Total Granulocytes	Total White Blood Cells
	1 (Immature)	2	3	4	5		
Minimum percentage....	0.0	1.0	4.5	2.0	0.0	14.0	5,900
Maximum percentage....	9.0	19.0	24.0	15.0	13.0	73.0	21,500
Average percentage.....	1.8	5.8	11.2	6.8	2.4	33.3	11,473

It seems probable that in a larger series the variations would have been considerably greater.

The various drawbacks to the use of Arneth's original classification have led to a large number of modifications. The most generally accepted and frequently utilized of these is the Schilling hemogram. Schilling and his followers have simplified Arneth's plan by dividing the neutrophils into myelocytes, juvenile forms, stab cells and well segmented mature polymorphonuclears. By charting the differential count in this order it is possible to retain Arneth's phrase of a shift to the left as representing an increase in immature forms. A further simplification, suggested by some authors, consists in using merely three classifications—myelocytes, unsegmented polymorphonuclears and segmented polymorphonuclears.[9] As will be seen, such a classification is not consistent with Schilling's concept of the difference in significance of the juvenile form as compared with the stab cell.

The Schilling hemogram and its various modifications are not subject to as much objection on the ground that they are cumbersome in routine work as is the Arneth index. Nevertheless the extra time and labor involved in making the differential count is sufficient to make one

wish to analyze rather carefully the amount and value of the added information gained by such a classification. A segmented neutrophil is described as a polymorphonuclear cell the nucleus of which is divided into two or more lobes connected by a thin filament of nuclear material. The stab or "rod-nuclear" cell is an unsegmented form in which the nucleus is elongated, bent in a U or S shape and perhaps slightly lobulated and shows irregular staining characteristics. Schilling considered this cell to be the result of some degenerative process which has prevented a healthy immature unsegmented neutrophil from going through the normal process of segmentation of the nucleus. Therefore he spoke of a "degenerative shift" when the shift to the left was made up largely of stab cells and of a "regenerative shift" when the increase was in myelocytes and juvenile forms. Schilling's juvenile neutrophil is an immature unsegmented form in which the nucleus is shaped more like a plump sausage which is curved or bent in various ways, is less pleomorphic, and the chromatin material of the nucleus is arranged more loosely. Actually, in the blood smears of infants one sees every gradation from the well segmented nucleus of the mature polymorphonuclear to the very immature neutrophil with a rounded or kidney-shaped nucleus. At one extreme it is sometimes difficult to say whether lobulation of the nucleus is sufficiently marked, the connecting band of nuclear material slender enough and the nuclear staining near enough to normal to enable one to class the cell as a true segmented mature polymorphonuclear. At the other end of the series it is hard to know how to differentiate between the stab cell with an unusually plump nucleus and a juvenile form with an unusually slender nucleus or between a juvenile form with a rather large nucleus and a myelocyte with a kidney-shaped nucleus. There is grave doubt as to whether most laboratory workers can make such differentiation with enough consistency or accuracy to justify the time spent. Even if the classification could be trusted there would still be doubt as to whether the cells classified as stab cells were degenerative forms or merely slightly immature polymorphonuclears the nuclei of which had not yet reached the stage of complete segmentation. In other words, many so-called stab cells may represent merely a transition form between the juvenile form and the mature neutrophil.

The study of the unstained living blood cell is much neglected in the average laboratory, although valuable information has been gained by such studies for many years. Schilling [10] stressed its importance as long ago as 1908, referring to it again in his textbook on the blood

10. Schilling, V.: Lebende weisse Blutkörperchen im Dunkelfeld, Folia haemat. **6**:429 (Dec.) 1908. Brugsch, T., and Schilling, V.: Die Kernform der lebenden neutrophilen Leukocyten beim Menschen, ibid. **6**:327 (Nov.) 1908.

picture.[11] In figure *7* is shown a series of semidiagrammatic sketches taken from a long series of actual drawings made while following under the microscope the ameboid wanderings of one three-lobed polymorphonuclear cell over a period of two hours.[12] Every effort was made to portray the apparent shape of the nucleus accurately. Some of the distortions of the nucleus are of particular interest in relation to the difficulty of carrying out either Arneth's or Schilling's method of classification. For example, in phases *8* and *10* (fig. *7*) the appearance was that of a two-lobed polymorphonuclear, owing, presumably, to the turning of the cell in such a way that one lobe was hidden behind the other. In phases *6* and *11* the cell might, perhaps, be classed as a stab cell, while even in phases *4* and *5* the appearance might lead to mistakes concerning the number of lobes or the filaments joining them. This series of sketches is not unlike a number of published drawings which depict different types of neutrophils.[13] When one makes a thin smear which dries immediately some cells may be caught in various phases of motion and in varying positions in relation to the angle at which the nucleus is viewed. Frequently a polymorphonuclear which is in reality well segmented may be fixed in such a position that a lobe is hidden or at least the connecting filament is not in view. An appreciation of the appearance of these cells when alive and moving helps one to avoid those mistakes in classification which come from the distortion of a normal mature cell.

After a long study of unstained fresh drop preparations, vitally stained drops and fixed smears prepared with various stains, it has seemed wise to confine the differentiation of the neutrophils to myelocytes, immature polymorphonuclears and mature polymorphonuclears (fig. 6). The immature polymorphonuclears in this classification correspond closely to the juvenile cell of Schilling, although there are times when other criteria suggest the designation of immaturity. In the next paper of this series the granulocytes are classified as has already been noted, but in view of the widespread use of the Schilling hemogram in diseased states [14] it seemed wise to publish here the results of

11. Schilling, V.: The Blood Picture, eds. 7 and 8, St. Louis, C. V. Mosby Company, 1929, pp. 38, 128 and 147.

12. With dark-field illumination a moving picture can be made which shows cell detail beautifully and allows one to study ameboid motions and the resulting distortions at leisure. Dr. H. M. Kingery gave me the opportunity to study such a film.

13. Needles, R. J.: A Neutrophilic Graph, J. Lab. & Clin. Med. **17**:962 (July) 1932. Schilling, Brugsch and Schilling.[10]

14. Rogatz, J. L.: The Schilling Blood Count in the Prognosis of Acute Infections in Infancy and Childhood, Am. J. Dis. Child. **40**:70 (July) 1930; **45**: 1022 (May) 1933. Nussbaum, S.: The Schilling Hemogram: Its Application in Pediatrics, Arch. Pediat. **49**:207 (April) 1932. McGee, W. A.: The Value of the Schilling Differential Count in Pediatrics, South. M. J. **25**:484 (May) 1932.

100 differential counts in which Schilling's type of classification was used. These data, like the reports of Gerard and Boerner,[15] Hoffman and Welcker[16] and others, are presented in order to show what variations may be considered consistent with good health. The counts were made for five healthy babies who were followed from birth to the age of 6 months at the Florence Crittenton Home. The majority of the counts fell in the age period of from 2 to 16 weeks. With a larger series the variations might have been even greater.

In table 2 an analysis is given of these 100 differential counts, using Schilling's classification. Since there was little correlation with age except for the high percentages of granulocytes in the new-born period, the analysis is based arbitrarily on the variations in range in the percentage of stab cells. These are arranged in descending order of total percentage of stab cells by intervals of 2 per cent. Because of the marked variation in the percentage of all the granulocytes at this age the stab cells are also tabulated as percentage of all the granulocytes. The myelocytes and juvenile forms are grouped together to facilitate the comparison between these known immature forms and the more doubtful stab cells. After the first month there was never a range for the myelocytes greater than from 0 to 1 per cent of the total count, or for the juvenile forms greater than from 0 to 3 per cent. From the second to the sixth month the range of myelocytes was from 0 to 0.5 per cent and that of the juvenile forms, from 0 to 1 per cent. A slightly higher range will be reported in a subsequent paper dealing with the analysis of 600 differential counts.

Comment.—I have no intention of minimizing the possible significance of immature cells as an aid in estimating the seriousness of certain infections or in giving a reliable prognosis in certain of the acute diseases of childhood. On the other hand, in any biologic process we must remember the necessity for familiarity with the entire run of variations which may be found during healthy function before attempting to interpret the variations observed during disorders. Furthermore, whether interpretations are made during health or illness, one must be cautious in arriving at conclusions concerning the fundamental causes or significance of the findings. And, finally, if one is to base conclusions on an accurate estimate of immature or abnormal cells in circulation during disease one must be reasonably sure that the cells so classified are actually immature or abnormal cells, and that they are

15. Gerard, J. H., and Boerner, F.: The Significance of a Shift to the Left in Differential Counts and Nuclear Index as a Means for Interpreting and Recording: Nuclear Index of Normal Blood and Influence of Age, J. Lab. & Clin. Med. **16**:300 (Dec.) 1930.

16. Hoffman, A., and Welcker, A.: Shifting to Left in Blood Picture in Diagnosis and Prognosis in Healthy Infants, Arch. f. Kinderh. **76**:1 (April) 1925.

TABLE 2.—*Analysis of the Extent of Variation and Average Percentage of Stab Cells Compared with the Percentage of Immature and Mature Neutrophils in One Hundred Counts on Five Healthy Babies During the First Six Months* *

Number of Instances	Age Range, Weeks	Stab Cells, Percentage		Stab Cells as Percentage of Granulocytes		Myelocytes and Juvenile Forms, Percentage		Segmented Polymorphonuclears, Percentage		Total White Blood Cells	
		Range	Average	Range	Average	Range	Average	Range	Average	Range	Average
1	0	26 to 27.9	26.00	32.5	32.50	19.5	19.50	33.5	33.5	24,200	24,200
0	.....	24 to 25.9	.....	....	.....	....	.....	....	....	.....	.....
4	0 to 1	22 to 23.9	22.20	27.6 to 34.0	30.10	1 to 21.5	11.60	34.5 to 39.5	37.0	17,500 to 34,450	24,150
1	4	20 to 21.9	20.00	38.0	38.00	1	1.00	29.5	29.5	20,200	20,200
2	0 to 2	18 to 19.9	18.70	26.3 to 39.3	32.80	1 to 8.5	4.75	16.0 to 48.0	32.0	10,250 to 18,500	14,375
3	0 to 4	16 to 17.9	16.60	22.0 to 30.9	26.00	1.5 to 6.0	4.00	34.0 to 52.5	44.1	15,900 to 21,500	19,033
0	.....	14 to 15.9	.....	.....	.....	....	.....	....	....	.....	.....
7	0 to 14	12 to 13.9	12.60	17.5 to 38.5	33.60	0 to 14.5	5.25	13.5 to 37.0	25.4	7,750 to 13,900	10,479
6	0 to 6	10 to 11.9	10.40	19.1 to 27.2	22.20	0 to 11.5	2.91	24.5 to 31.5	28.4	10,200 to 15,900	13,666
8	0 to 16	8 to 9.9	8.50	18.2 to 42.5	26.90	0 to 11.0	2.37	9.0 to 39.0	21.2	6,700 to 14,450	10,612
14	2 to 18	6 to 7.9	6.50	9.7 to 25.0	17.20	0 to 5.0	1.10	14.5 to 49.0	26.5	7,000 to 19,650	12,932
19	3 to 18	4 to 5.9	5.04	9.7 to 28.1	15.70	0 to 4.5	1.05	8.5 to 34.0	23.4	7,500 to 19,200	12,789
19	4 to 24	2 to 3.9	2.80	5.4 to 24.1	9.80	0 to 1.5	0.28	8.5 to 43.0	22.1	8,100 to 18,150	12,995
16	5 to 24	0 to 1.9	0.80	0 to 6.4	2.80	0 to 0.5	0.06	10.5 to 34.0	20.2	5,900 to 16,800	11,940
Total 100	0 to 24	0 to 26.0	6.83	0 to 42.5	16.45	0 to 21.5	1.96	8.5 to 52.5	24.8	5,900 to 34,450	13,274

* Arranged according to the descending order of the percentage of stab cells.

present in numbers greater than may be seen during the healthy functioning of that organism.

There is no question that the typical stab or rod nuclear cell of Schilling may be differentiated from the segmented polymorphonuclear in many instances if a reasonable degree of care and time is used. That the majority of cells so classified in the average laboratory are actually either degenerate or significantly immature forms is open to question. In the first six months of infancy these cells may vary in number from 0 to 42.5 per cent of all the granulocytes (table 2). In other words, they may be present in relatively large numbers in a healthy infant. The count on the blood of one baby showed a variation from 0.5 to 6.5 per cent (from 1.5 to 17.5 per cent of the granulocytes) during one day. Whether or not one accepts these facts as evidence that they are abnormal cells, at least their presence argues against the fact that the stab cell is of much pathologic significance in infancy. In contrast with this situation the definitely immature cells (juvenile forms and myelocytes) are more surely classified, are not present in such large numbers in healthy infants and show considerably smaller fluctuations. For these reasons I feel justified in stating that during infancy it is more sensible to limit the division of the neutrophils into myelocytes, immature polymorphonuclears and mature polymorphonuclears, attaching significance only to marked fluctuations in the numbers of the first two groups.

The figures noted in table 2 as the upper limits for the stab and immature cells might well point to the presence of disease in an older child or an adult. It would be assumed that the presence of these cells indicated a severe infection or that their increase could be taken as an indication of the severity of some pathologic process. The occurrence of these cells in the healthy infant should serve as a warning that one must consider other factors in accounting for their presence in the peripheral blood. When there is either a physiologic or a pathologic demand for more leukocytes in the circulation it would seem that the number of immature forms must depend in part on whether or not there is sufficient active leukopoietic tissue to satisfy this demand entirely with mature cells. Individual variations in the amount and efficiency of the leukopoietic tissue must play some part in the variation in the number of immature cells found in different persons from apparently similar stimuli. In the small infant the demand for circulating leukocytes may have a more or less constant tendency to be greater than the available supply of mature leukocytes furnished by the young leukopoietic tissue. During the growth and development of the first few years a balance between the supply and demand may be acquired, but even then an unusually heavy demand may overtax the ability of the

leukopoietic tissue so that immature cells are delivered into the circulation more easily than in the mature organism. Much study is needed before there is a complete understanding of this mechanism. The healthy infant offers an excellent opportunity for studying immaturity in cells without the complications brought about by the presence of disease.

SUMMARY AND CONCLUSIONS

The routine technic and classification used in differential white blood cell counts have been compared with more specialized methods.

The first study consisted in comparing 100 differential counts on fixed smears prepared with Wright's stain with the same number of counts performed on fresh drop preparations supravitally stained.

Charts are presented which show the variation in the percentage of each cell type in comparing: (1) differential counts on preparations stained with the vital stain and with Wright's stain, (2) a second series of counts on preparations stained with Wright's stain and (3) the average of these two counts on preparations stained with Wright's stain with the counts on preparations prepared with the vital stain.

There was no constant or striking tendency for any one cell type to appear more frequently in the fresh drop preparation than in the fixed smear or vice versa.

The deviations noted in each of the three sets of comparisons were greater than those usually given, being smallest for the comparison of the first and second series of counts on the fixed smears prepared with the Wright stain.

From this study it was concluded that a fixed smear stained with a reliable Wright's stain may show the same distribution of white blood cells in infant's blood as is shown in a fresh drop stained with neutral red and janus green B.

The second study consisted in a critical analysis of the Arneth, Schilling and similar classifications of the granulocytes.

Tables are given to show the variations which were found in a small group of healthy infants when the various methods were used.

The uncertainty of classification as well as the time-consuming nature of the procedure are felt to overbalance any value gained by grouping the neutrophils according to the number of nuclear lobes.

By Schilling's method the lack of constancy and reliability in classification as well as the amount of variation found are much greater for the stab cell than for the more definitely immature juvenile form or myelocyte.

It was concluded that in the young infant the simplest, safest and most significant classification of the granulocytes is accomplished by divid-

ing them into groups of myelocytes, immature polymorphonuclears, polymorphonuclears, eosinophils and basophils.

For routine work and for most practical purposes in clinical medicine the routine method of staining and counting the white blood cells seems to be as satisfactory and safer than the special methods studied. This is based on the assumption that the smear is carefully made, the Wright stain of good quality and the count done thoroughly and honestly.

BLOOD CELLS IN HEALTHY YOUNG INFANTS

III. A STUDY OF 608 DIFFERENTIAL LEUKOCYTE COUNTS, WITH A FINAL REPORT ON 908 TOTAL LEUKOCYTE COUNTS

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The first paper [1] of this series dealt with the hourly and daily variations in the total leukocyte counts of six healthy infants during the first three months of life. The purpose of the study as a whole has been to find out what variations from the so-called normal are consistent with health in contrast with those which point inevitably to the presence of some disease process. The second contribution [2] was a critical analysis of certain specialized technics, methods and classifications which may be utilized in differential white blood cell counts. As a result of this study it is felt that the routine method described in the first paper [1] not only yields satisfactory results but actually represents the method of choice for most practical purposes when every angle of the problem is considered. Although the possible errors are relatively large, the distribution of the "plus" and "minus" deviations is fairly well balanced. Hence it would seem that the long series of counts on individual babies would tend to minimize their effect in obtaining the picture of variations in any one subject from time to time or between two babies in the same age period. Consequently, in this third contribution I present the picture of individual variations in the differential leukocyte counts of healthy infants during the first six months of life as shown by the usual routine method with the fixed smear and Wright's stain.

MATERIAL AND METHOD OF STUDY

Twenty healthy babies in the nursery of the Florence Crittenton Home were utilized for carrying out this study of the leukocytes. On the first seven babies in the series from 1 to 3 counts per week were made for periods varying from two to twenty weeks. The counts on the eighth baby, with three series of hourly counts, showed such striking fluctuations as to lead to the adoption of this method

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From the Child Research Council and the University of Colorado School of Medicine.

1. Washburn, A. H.: Blood Cells in Healthy Young Infants: I. The Leukocytic Picture During the First Three Months with Special Reference to Hourly and Daily Variations, Am. J. Dis. Child. **47**:993 (May) 1934.

2. Washburn, A. H.: Blood Cells in Healthy Young Infants: II. A Comparison of Routine and Special Technics in the Differentiation of Leukocytes, Am. J. Dis. Child., this issue p. 395.

of study in the remaining cases. In the last twelve babies counts were made at 9:00, 10:00, 11:00 a. m. and 12:00 noon and at 2:00, 3:00, 4:00 and 5:00 p. m. on a series of single days at intervals varying from one to five weeks. The study of cases 9 to 14 formed the basis for the first report.[1] The present report on the differential leukocyte counts is based on a study of cases 14 to 20, while the final report on total counts, included here, represents a résumé of the counts on all twenty babies. The duration of the follow-up period in cases 14 to 20 was twenty-five, forty-eight, twenty-four, fifteen, fourteen, twenty-six and twelve weeks, respectively. The number of individual counts for each of these babies was 110, 109, 103, 78, 48, 96 and 64, respectively. Of this total number of 608 counts 73 were made in the new-born period and 535 between the second and twenty-sixth week.

The nursing care of these babies, their feeding and their entire twenty-four hour regimen remained the same as was described in the previous report.[1] As in the start of this series of studies, every attempt was made to duplicate average healthy conditions and to obtain the picture of variations during health in a way consistent with good medical practice. The technic and schedule described were continued, with blood drawn hourly from alternate heels. A total white blood cell count was done each time, and smears were made for examination on the following day. At least one and sometimes two red blood cell counts and determinations of hemoglobin were done each day during the study of the leukocytes. Except for the special stains and technics described in the second paper,[2] which were used for preparations of the blood of the same infants, all the differential counts were done on fixed smears, made on cover-slips and stained with Wright's stain. Every differential count reported in this paper was done with this routine technic. A minimum of 200 cells was always counted, care being taken to sample the entire cover-slip smear. When the count of the first 100 cells, made on one half of the cover-slip, failed to check closely with the second 100, another 100 cells were counted. If the count of the third 100 failed to fall between the first and second, a fourth 100 was counted for the final average. The majority of the counts included only 200 cells.

CLASSIFICATION OF THE LEUKOCYTES

Before presenting the results of the analysis of these differential counts it may be well to describe the routine classification which has been used. The photomicrographs reproduced as figure 1 in the first paper [1] and as figure 6 in the second [2] together with figures 1 and 2 in this report show the various cell types described. The reader is referred to these four reproductions for illustrations of the descriptions which follow.

The Bone Marrow Group or Granulocytes.—There is, of course, no great difficulty in classifying eosinophils and basophils. The neutrophils have been divided into myelocytes, immature polymorphonuclears and mature polymorphonuclears. The mature polymorphonuclear is familiar in its typical form with a well segmented nucleus of from two to six lobules joined by narrow bands of nuclear material and with its neutrophilic granular cytoplasm. In this study no attempt has been made to split hairs over the question of minor variations in the maturity of the neutrophil as shown by the number of nuclear lobes or by the

completeness of their segmentation, a complete discussion of which was given in the second paper of the series.[2] The immature polymorphonuclear is usually slightly larger; its nucleus is unsegmented, though it may be somewhat lobulated; it is plump and relatively vesicular in appearance and presents a shape which varies from a shallow U or

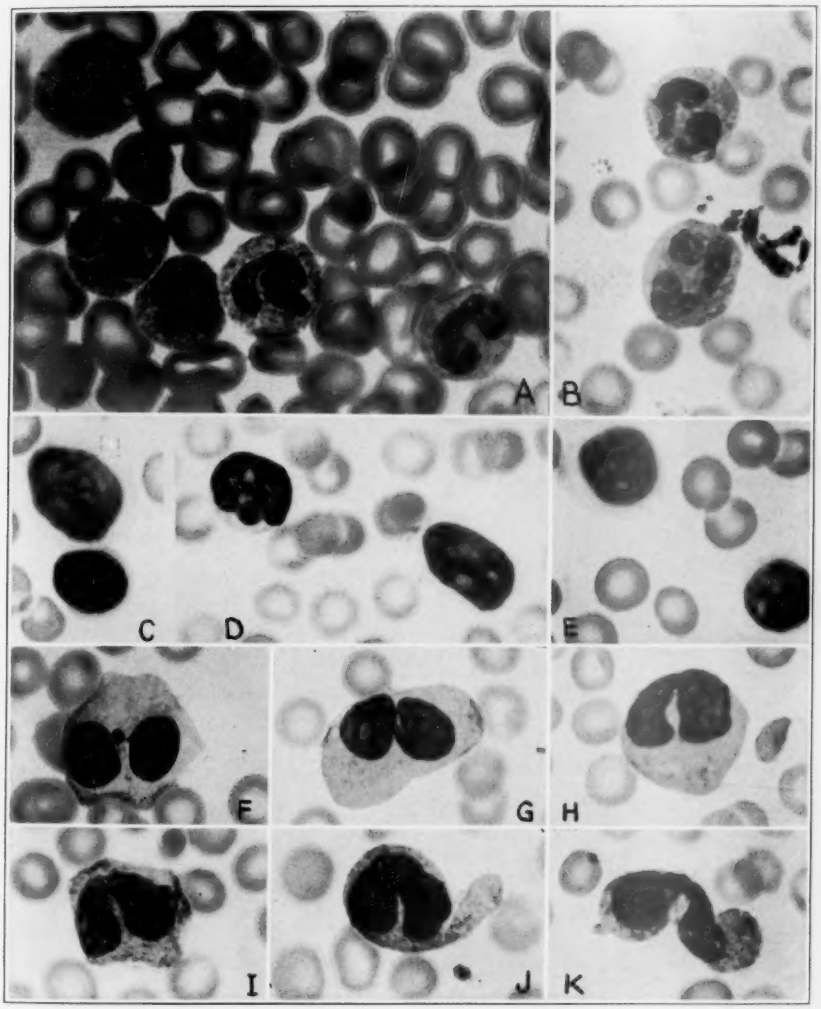

Fig. 1.—Characteristic leukocytes from blood smears of the subjects in cases 15 to 20. *A* and *B* depict varying degrees of maturity in neutrophils; *C*, *D* and *E*, contrasts between large, intermediate and small lymphocytes; *F*, *G* and *H*, varying degrees of segmentation in the nuclei of monocytes; *I* shows a common monocyte of the granular type, and *J* and *K* depict ameboid motion of granular monocytes as indicated even in fixed smears. Wright's stain.

irregular S to that of a rather slender kidney. This group corresponds most closely to Schilling's juvenile cell and may, perhaps, include a few cells which he would classify as stab cells. The myelocyte is usually fairly characteristic, being approximately the same size as the immature polymorphonuclear, with a round or plump kidney-shaped nucleus and with distinctly more tendency to a basophilic reaction in the granular cytoplasm. The only cell with which it is likely to be confused is an unusually granular monocyte, which will be described under that heading.

Lymphocyte Group.—The lymphocyte is the predominant cell in the blood of the infant from some time between the second and the sixth week throughout the first half year. A comparison of the blood of the older child or adult and that of the infant shows that the lymphocytes differ not simply in the numbers present but also in the type of cell which is most often found. The typical small lymphocyte of adult blood is not the most characteristic member of the group in early infancy. In a large series, on dividing the lymphocytes into large and small types one finds approximately equal numbers of each. Even these figures fail to give an accurate picture of the situation, because a large proportion of the lymphocytes are intermediate in size between the real small lymphocyte of the adult and the definitely large type which measures from two to three times the diameter of an erythrocyte. This makes the differentiation into large and small types very uncertain, since one's estimate of exact size does not remain constant from day to day. For this reason all the lymphocytes have been grouped together in the figures. Almost the only possible error in the classification of the lymphocytes is due to the occasional confusion between atypical monocytes and atypical large lymphocytes. This will be considered in the following paragraph.

Monocyte Group.—The variety of mononuclear forms depicted in figure I suggests, probably correctly, that the monocytes form a rather heterogeneous group. The so-called typical member of the group is slightly larger than a mature neutrophil and has a slate-gray background containing fine pinkish granules which tend to occur in groups. Its nucleus is large and roughly kidney-shaped and stains a paler purple than that of either the lymphocyte or mature neutrophil. The arrangement of the nuclear material is more complex. Rather less than half the monocytes seen in the blood of the young infant belong in this category. An almost equal number show varying amounts of coarse granulation, usually purplish and sometimes, though not always, obscuring the characteristic cytoplasm. The nuclei of these cells are apt to be more deeply stained and present almost every shape from a round or slightly indented to a truly segmented form with two distinct lobes. This is the type of monocyte which may be difficult to differentiate from the myelocyte or immature neutrophil. Ordinarily, however,

characteristic gray cytoplasm and pinkish granulation of the monocyte can be made out. A combined peroxidase and Wright's stain may give definite assistance in this differentiation.[2]

Another less common but not unusual type of monocyte is the agranular form. These cells present a cytoplasm which is slightly more bluish than that of the traditional monocyte and which may contain no granules or, at best, only a few very fine ones. The nucleus may be round, kidney-shaped or actually bilobed (fig. 1). When such a cell is seen in the same field with a large lymphocyte it will be noted that the cytoplasm of the monocyte is not quite so blue or as homogeneous in consistency and that its nucleus shows a more complex arrangement of the chromatin with paler staining. When seen alone it may be mistaken easily for a large lymphocyte. Actually, even in the blood of one infant every gradation from the agranular to the typical monocyte and from the typical to the very granular form may be seen.

Immature Cells.—Those cells which are definitely less mature than a myelocyte or than a very large but still recognizable lymphocyte have been grouped together under the label of blast cells. No attempt has been made to divide them into lymphoblasts, myeloblasts or, possibly, monoblasts. They all show a very deep blue agranular but fuzzy cytoplasm with a large round or oval nucleus which may be eccentric. The diameter varies from two to five times that of a red blood cell. There is also considerable variation in the compactness of the arrangement of chromatin in the nucleus, although the nuclei of all these cells stain deeply. Sometimes the nucleus appears as an almost solid homogeneous mass, at times as though arranged in whorls and at other times as though a solid mass had been fractured in many places (fig. 2). The latter type resembles a megaloblast. These blast cells, however, are not seen as often in the new-born period as they are between the fourth and eighth weeks. Since the new-born period is the time when the myelocytes are seen in greatest numbers and since the period from 4 to 8 weeks represents the time of marked increase in the lymphocytes, it is felt that a majority of the blast cells are probably lymphoblasts.

Unclassified Cells.—There are apt to be from 0.5 to 2 per cent of the leukocytes which I am unable to classify. These are mostly mononuclear forms and probably represent a heterogeneous group of atypical cells, some of which are surely immature forms and some of which may represent degenerate forms, although they are apparently whole, functioning cells. In this group there is only one cell type which has been seen repeatedly and which therefore ought to be classifiable. This is a very large cell (fig. 2) with a pale grayish-blue cytoplasm studded with rather small and extremely discrete purple granules which resemble most closely those seen in the platelets. Its nucleus appears to be very complex in structure and stains a pale purple or lavender in the average

preparation with Wright's stain. It usually occurs during the first six weeks of life but is quite as apt to appear in smears which contain few or no myelocytes as in those with many. When compared with

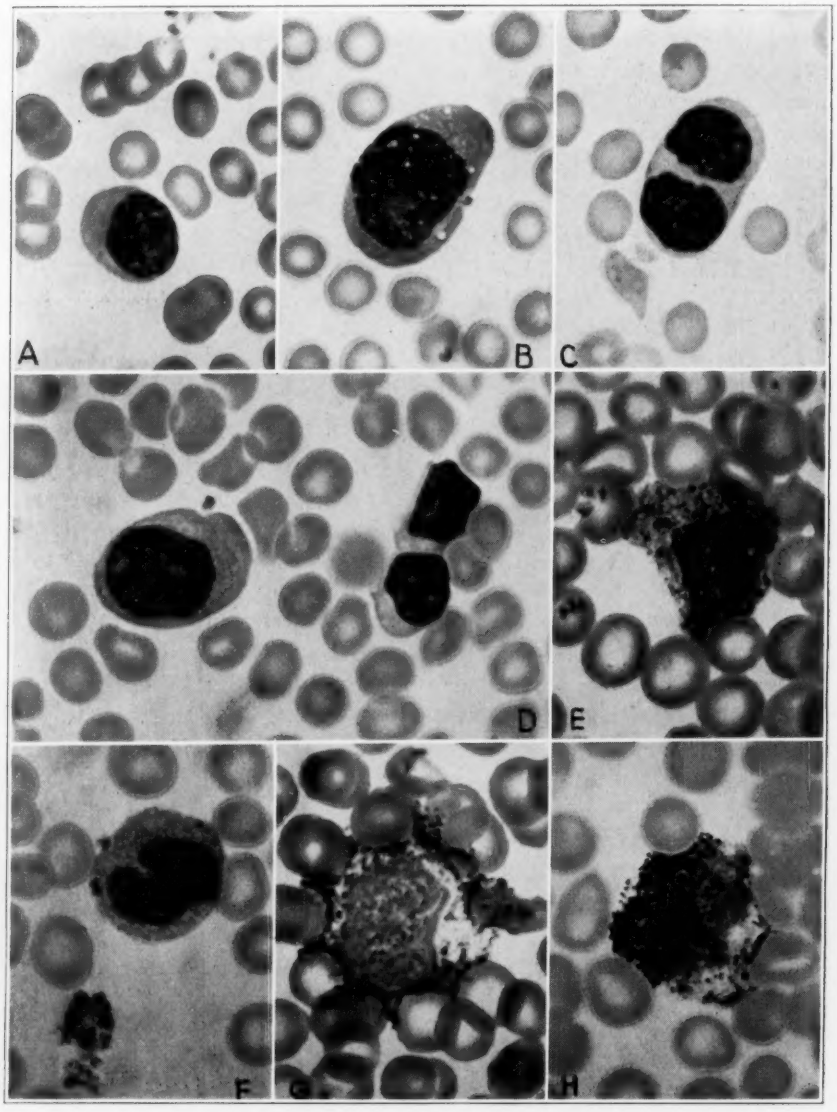

Fig. 2.—A group of immature and unclassified leukocytes from the subjects in cases 14 to 20. *A* depicts a small blast cell; *B*, a very large blast cell which shows characteristics of an extremely primitive cell; *C*, mitosis in a blast cell, and *D*, a large blast cell compared with two intermediate lymphocytes; *E*, *F*, *G* and *H* are illustrations of an unusual cell type described in the text as unclassified. Wright's stain.

myelocytes in the same smear its characteristics are strikingly different. The granules are smaller, more discrete and more purplish than those of either a basophil or a basophilic myelocyte. The possibility of its being a megakaryocyte is being given serious consideration.

ANALYSIS OF 608 DIFFERENTIAL LEUKOCYTE COUNTS

Of the total of 608 complete differential leukocyte counts 73 were made during the new-born period (from birth to the tenth day), and 535 were made between the second and twenty-sixth week of life. Since, as is well known, both total and differential counts in the new-born differ greatly from those later in infancy, it seemed best to present the analyses in two separate tables. Because of the large amount of work already done on the leukocytic picture of the new-born the major emphasis of my study has been placed on findings during the remainer of the first six months. Nevertheless, the transition from the condition existing at birth to that later in infancy presents an interesting picture and one the characteristics of which are hard to visualize from two separate tables of figures. Moreover, the hourly and daily fluctuations in the various cells in any one infant are not apparent in the tables. In order to give as complete a picture as possible of all these variations in healthy infants I have presented: (1) table 1, showing the minimum, maximum and average figures for each type of cell in each baby during the new-born period; (2) table 2, showing corresponding data for the age period from 2 to 26 weeks; (3) figure 3, depicting the hourly counts on selected days from birth to 24 weeks in case 16, and (4) figure 4, presenting the same picture of hourly fluctuations from birth to 23 weeks in case 19. A careful study of these tables and figures will yield most of the observations resulting from this investigation. A few comments about each may serve to emphasize some of the more significant points which are brought out.

Before discussing the tables and charts one point, already noted in the first paper of this series, deserves second mention. It is misleading to present the figures for the differential count only in terms of percentage. For example, let it be assumed that the upper limit for the lymphocytes in one case was 80 per cent while in a second case it was 60 per cent. Let it also be assumed that in the first case the total leukocyte count was 10,000 per cubic millimeter at the time when there were 80 per cent lymphocytes, while in the second case there were 20,000 leukocytes per cubic millimeter when there were 60 per cent lymphocytes. Actually, then, the upper limit for the lymphocytes in the first case was 8,000 per cubic millimeter, as against 12,000 in the second case. That is, in the case in which the smaller percentage occurred there were half again as many lymphocytes in circulation as in the case in which the percentage was larger. With variations of as much as 10,000 in the

white blood cell counts during the hours of one day it is easy to see the importance of presenting not merely the percentage of each type of cell but also the total number per cubic millimeter. In tables 1 and 2 both the percentage and the total number of white blood cells are given, since it was often true that the minimum or maximum percentage and the minimum or maximum total number were not found in the same count. In figures 3 and 4 only the actual number of white blood cells per cubic millimeter is given, in order that the curve may be compared more easily with that of the total number per cubic millimeter.

In table 1 the expected preponderance of granulocytes over lymphocytes is seen when the average percentages for all the counts on the six babies studied in the new-born period are examined. However, if the average figures for each individual baby are examined a marked variation is apparent. Thus, in case 18 there was an average of 74.1 per cent or of 11,401 granulocytes per cubic millimeter, as compared with 19.6 per cent or 2,921 lymphocytes, while in case 17 there were only 50.2 per cent or 4,500 cells of bone marrow origin, as against 41.1 per cent or 3,688 lymphocytes. An estimate of the total amount of variation found in all the 73 counts on these six babies may be had by comparing the minimum and maximum figures for these two major groups of cells. The variation in the granulocytes is seen to be from 36.5 to 86.5 per cent or, in terms of total cells per cubic centimeter, from 2,740 to 27,328. Incidentally, these figures may serve as a nice illustration of why it is not safe to trust a record given only in terms of percentages. The count for every cell type classified tells the same story of individual variations during health.

In table 2 one notes at once the shift to lymphocytic preponderance. Here again the difference in the counts for individual babies is striking. For example, in case 18, in which the percentage of granulocytes showed the highest average in the new-born period, there occurred both the highest average percentage (41.8) and the highest total count (5,362). In case 17 there occurred the lowest average for granulocytes (23.8 per cent) and the highest average percentage for lymphocytes (70 per cent), although interestingly enough there were three other babies whose blood showed a higher average number of lymphocytes per cubic millimeter. In case 19, which showed the next highest average for total lymphocytes in the new-born period occurred the highest average number given in table 2. A study of the difference between the minimum and maximum counts for the polymorphonuclear neutrophils also serves to bring out the presence of striking individual variations. In case 14 there was a range of 49.5 per cent and 5,841 cells per cubic millimeter; in case 19, a range of 42.9 per cent, but 8,460 cells, and in case 20, a range of only 26 per cent and 4,198 cells. The possible variation in the number of lymphocytes appears to be from 2,322 to 15,717 per cubic

TABLE 1.—*Minimum, Maximum and Average Figures for Each Cell Type in the Blood of Six Healthy Infants During the First Ten Days of Life* *

		Polymorphonuclears										Lymphocytes												Total White Blood Cells
		Mature		Immature		Myelocytes		Eosinophils		Basophils		Large		Small		Monocytes		Blast Cells		Unclassified Cells		All Granulocytes		All Lymphocytes		
	Case	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Number per Cu. Mm.
Minimum	14	27.5	2,096	1.5	96	0	0	3.0	225	0	0	10.0	1,024	8.5	684	6.0	416	0	0	0	0	36.5	2,740	21.0	1,760	6,400
	16	31.5	3,152	3.0	379	0.5	102	1.5	183	0	0	2.5	491	6.0	1,539	2.0	430	0	0	0	0	45.0	4,973	9.5	2,436	9,850
	17	33.5	2,428	2.0	145	0	0	3.5	253	0	0	10.6	932	12.5	934	3.0	307	0	0	1.0	72	39.0	2,826	28.5	2,130	7,250
	18	48.6	5,159	2.0	212	0	0	2.3	247	0	0	4.5	618	7.5	1,031	2.0	280	0	0	1.0	140	54.3	5,759	12.0	1,650	10,600
	19	56.5	8,280	3.3	483	0	0	1.5	252	0	0	9.0	1,834	7.0	1,225	2.0	316	0	0	2.0	345	64.5	9,453	19.0	3,269	13,800
	20	30.5	4,387	6.0	844	4.0	540	0	0	0	0	0.5	143	9.5	2,293	0	0	0	0	0	0	44.5	6,338	13.2	3,522	12,550
	All	27.5	2,096	1.5	96	0	0	0	0	0	0	0.5	143	6.0	684	0	0	0	0	0	0	36.5	2,740	9.5	1,650	6,400
Maximum	14	58.5	6,552	4.0	416	2.5	220	9.0	1,008	2.00	167	36.5	2,865	21.0	1,848	11.0	960	1.0	64	3.5	312	71.0	7,952	50.0	4,512	11,200
	16	71.0	18,211	9.0	2,308	5.5	672	9.0	1,277	1.50	294	28.5	3,961	25.0	4,558	10.5	1,459	2.0	271	3.5	491	86.5	20,186	45.5	6,764	25,650
	17	48.5	4,663	4.5	512	1.0	102	7.5	574	2.00	156	29.5	2,994	28.0	2,870	9.5	693	0.5	50	6.5	678	60.5	5,685	53.5	4,973	10,450
	18	69.5	14,178	6.0	1,224	1.0	204	7.0	1,224	0.50	70	16.6	1,836	22.6	2,958	6.0	990	0	0	3.0	460	81.0	16,320	39.3	4,794	20,400
	19	66.5	20,282	6.0	1,830	1.3	305	5.0	925	1.50	252	20.5	3,417	16.0	3,050	5.5	877	0	0	5.0	875	76.5	23,331	30.0	5,795	30,500
	20	57.5	19,062	22.5	6,201	8.5	2,146	6.5	1,332	0.70	154	26.2	3,833	30.5	5,459	6.0	1,230	0.7	93	3.5	665	84.0	27,328	47.0	8,756	34,450
	All	71.0	20,282	22.5	6,201	8.5	2,146	9.0	1,332	2.00	294	36.5	3,961	30.5	5,459	11.0	1,459	2.0	271	6.5	875	86.5	27,328	53.5	8,756	34,450
Average	14	41.1	3,532	2.7	233	0.5	46	6.4	544	0.80	67	24.4	.....	13.2	.....	8.9	742	0.2	14	1.5	129	51.6	4,429	37.7	3,143	8,461
	16	48.4	8,622	6.4	1,122	2.0	320	4.7	746	0.60	105	12.8	.....	17.3	.....	5.4	828	0.3	32	1.7	279	62.3	10,736	30.2	4,381	16,685
	17	41.1	3,689	2.8	256	0.4	36	4.7	469	0.60	49	19.7	.....	21.3	.....	6.3	543	0.1	6	2.2	212	50.2	4,500	41.1	3,688	8,221
	18	64.3	9,869	4.0	642	0.6	97	4.9	779	0.10	13	8.7	.....	10.8	.....	4.1	626	0	0	2.1	312	74.1	11,401	19.6	2,921	15,268
	19	60.2	11,739	4.5	904	0.5	120	3.5	663	0.30	71	13.8	.....	10.1	.....	3.2	609	0	0	3.3	630	69.5	13,523	24.0	4,550	19,306
	20	45.4	10,424	12.7	3,140	6.3	1,373	2.3	416	0.20	42	10.7	.....	18.0	.....	2.5	451	0.1	10	1.4	298	67.6	15,397	28.8	5,778	21,812
	All	48.3	7,769	6.1	1,185	2.2	410	4.4	591	0.45	62	15.5	.....	15.4	.....	5.3	648	0.1	13	1.9	283	61.7	9,984	31.0	4,237	15,208

* The same figures for all seventy-three leukocyte counts are included.

TABLE 2.—*Minimum, Maximum and Average Figures for Each Cell Type in the Blood of Each of Seven Healthy Infants Between the Second and Twenty-Sixth Week of Life* *

		Polymorphonuclears										Lymphocytes												Total White Blood Cells
		Mature		Immature		Myelocytes		Eosinophils		Basophils		Large		Small		Monocytes		Blast Cells		Unclassified Cells		All Granulocytes		All Lymphocytes	
	Case	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Percentage	Number per Cu. Mm.	Number per Cu. Mm.
Minimum	14	13.5	1,081	0	0	0	0	1.5	195	0	0	7.0	1,029	7.0	602	1.5	210	0	0	0	0	16.5	1,633	27.0	2,322	5,700
	15	8.7	796	0	0	0	0	0	0	0	0	9.5	815	12.0	1,326	1.5	200	0	0	0	0	9.7	886	41.0	3,907	6,650
	16	5.0	417	0	0	0	0	1.0	62	0	0	14.5	1,094	13.3	951	2.0	213	0	0	0	0	10.5	651	39.0	3,061	5,900
	17	6.5	679	0	0	0	0	0	0	0	0	16.0	1,206	21.0	1,522	2.0	162	0	0	0	0	10.5	987	44.0	3,190	6,700
	18	17.0	1,436	0	0	0	0	0.5	64	0	0	14.3	1,530	9.5	935	3.0	363	0	0	0	0	26.5	2,533	28.3	3,736	7,750
	19	8.6	1,034	0	0	0	0	0	0	0	0	18.0	2,126	5.0	795	1.0	146	0	0	0	0	12.5	1,896	32.5	4,525	9,050
	20	11.5	1,181	0	0	0	0	0.5	39	0	0	12.5	1,362	18.0	2,457	3.0	273	0	0	0	0	16.5	1,451	47.5	4,823	7,800
	All	5.0	417	0	0	0	0	0	0	0	0	7.0	815	5.0	602	1.0	146	0	0	0	0	9.7	651	27.0	2,322	5,700
Maximum	14	63.0	6,922	4.50	491	2.50	229	13.0	1,842	2.00	175	58.5	8,745	61.0	10,130	18.0	1,638	2.00	266	3.00	309	68.0	8,578	78.5	14,312	22,900
	15	46.5	7,409	3.00	507	1.50	203	6.5	1,056	2.50	385	52.5	8,439	68.0	11,492	13.0	1,599	2.50	388	2.00	249	51.0	9,032	88.0	14,744	20,300
	16	39.0	5,376	3.50	418	2.00	279	13.0	1,536	3.00	360	59.5	10,438	48.5	6,785	10.5	1,418	1.50	188	2.00	310	53.0	6,486	84.5	13,525	22,400
	17	39.0	5,183	4.00	290	0.50	55	11.0	1,760	1.00	192	48.0	8,544	54.5	6,825	10.5	1,533	2.50	250	2.00	282	47.5	6,177	86.0	13,338	19,200
	18	50.0	8,925	6.00	762	2.50	255	15.5	2,681	2.00	267	46.5	8,671	31.6	4,052	15.0	2,265	2.00	257	3.50	624	64.0	11,155	63.5	12,723	18,850
	19	51.5	9,494	6.00	1,314	4.00	510	15.0	1,580	1.50	265	50.0	8,950	56.0	10,123	12.5	2,412	2.00	322	3.00	624	58.5	11,514	84.2	14,320	24,150
	20	37.5	5,379	3.00	556	3.50	546	8.0	992	2.50	258	44.5	6,048	59.0	10,377	13.0	2,028	2.50	303	3.50	649	46.0	7,047	80.0	15,717	20,800
	All	63.0	9,494	6.00	1,314	4.00	546	15.5	2,681	3.00	385	59.5	10,438	68.0	11,492	18.0	2,412	2.50	388	3.50	649	68.0	11,514	88.0	15,717	24,150
Average	14	27.5	3,105	1.07	117	0.20	20	5.5	631	0.40	46	28.2	.....	29.5	.....	5.3	705	0.50	34	0.50	49	34.7	3,880	57.6	6,628	11,314
	15	23.8	2,923	0.54	74	0.08	10	1.9	239	0.25	43	27.7	.....	38.4	.....	5.7	695	0.40	44	0.40	43	26.9	3,305	65.7	8,070	12,162
	16	21.5	2,325	0.31	37	0.13	16	6.3	678	0.68	73	34.2	.....	30.1	.....	5.6	605	0.30	25	0.20	28	29.2	3,111	64.4	6,809	10,709
	17	19.2	2,257	0.46	44	0.02	2	3.6	435	0.39	45	34.9	.....	35.5	.....	5.2	582	0.50	58	0.30	32	23.8	2,630	70.0	7,895	11,179
	18	33.0	4,241	2.20	265	0.23	26	5.8	765	0.49	64	31.1	.....	18.1	.....	7.4	916	0.50	60	0.90	123	41.8	5,362	49.2	6,257	13,000
	19	26.3	3,995	0.98	162	0.32	44	3.8	564	0.28	42	29.7	.....	30.6	.....	4.7	1,031	0.50	78	0.50	74	31.7	4,708	60.3	8,911	14,965
	20	22.0	2,755	0.88	116	0.50	71	4.0	479	0.82	100	24.6	.....	39.1	.....	6.6	828	0.50	75	0.70	89	28.2	3,524	63.8	7,934	12,420
	All	24.4	3,024	0.81	104	0.19	24	4.31	518	0.45	55	30.1	.....	32.4	.....	5.6	751	0.46	51	0.45	56	30.2	3,691	62.4	7,582	12,196

* The same figures for all five hundred and thirty-five complete leukocyte counts are included.

millimeter, while for the mature neutrophils it is from 417 to 9,494. These variations are somewhat wider than those noted by Fletcher and Mitchell,[3] who gave from 500 to 8,500 as the variation for the polymorphonuclears and from 2,000 to 10,500 as that for the lymphocytes (for further comparisons with the literature the reader is referred to the two previous papers in this series). The figures for the monocytes demonstrate the fallacy of trusting to averages in estimating the normal situation. An examination of the average figures for each baby shows a marked degree of constancy at about 5.5 per cent, and yet the total amount of variation for all 535 counts runs from 1 to 18 per cent or

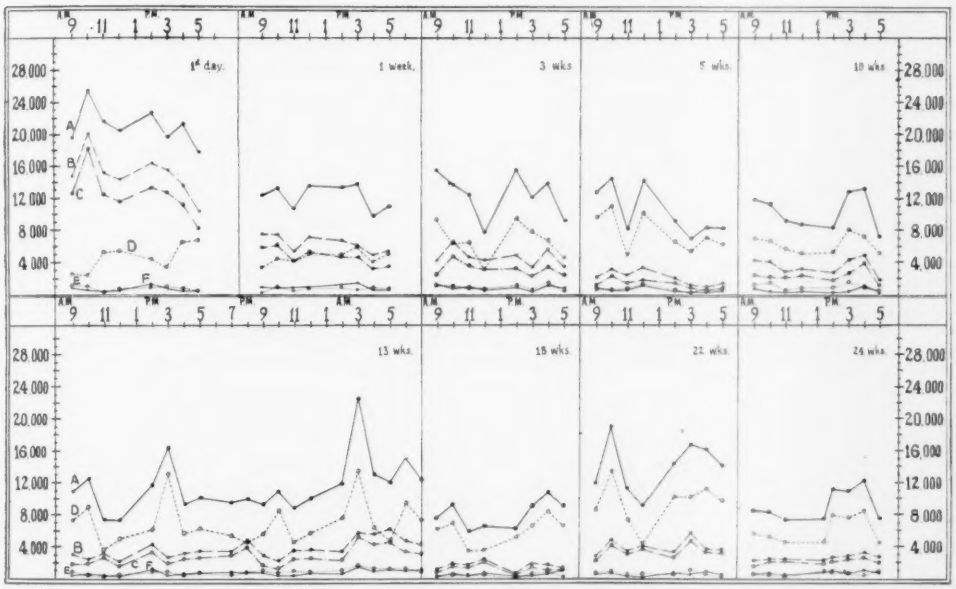

Fig. 3.—Curves depicting the hourly fluctuations of all the leukocyte counts on selected days between birth and the sixth month in case 16. In this and the following figure the curve indicated by the unbroken line (*A*) represents the total white blood cell count: the long dashes (*B*), all the granulocytes; the long dashes and dots (*C*), the polymorphonuclears; the short dashes (*D*), all the lymphocytes; the dotted line (*E*), the eosinophils, and the unbroken line (*F*), the monocytes.

from 146 to 2,412 monocytes per cubic millimeter. The counts for eosinophils show marked variations whether the figures for individual averages or for the whole range are compared. These few examples may serve to demonstrate the character of the data contained in tables 1 and 2.

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3. Fletcher, E. G., and Mitchell, A. G.: Physiologic Variations in the Leukocytes in Infants and Children, Am. J. Dis. Child. **34**:807 (Nov.) 1927.

In figure 3, 84 of the 103 complete differential counts in case 16 are shown in graphic form. This enables one to follow the hourly fluctuations in the number of each of the important types of leukocytes in relation to those of the total count. Curves are included of the counts for eight different days and for one twenty-four hour period between birth and the sixth month. All the 608 counts on the seven babies have been charted in this manner for purposes of study. The figures for case 16 and case 19 (fig. 4) have been selected for presentation because they seem to show most of the characteristics of the group as a whole; a comparison of the two figures will bring these out. The condition in

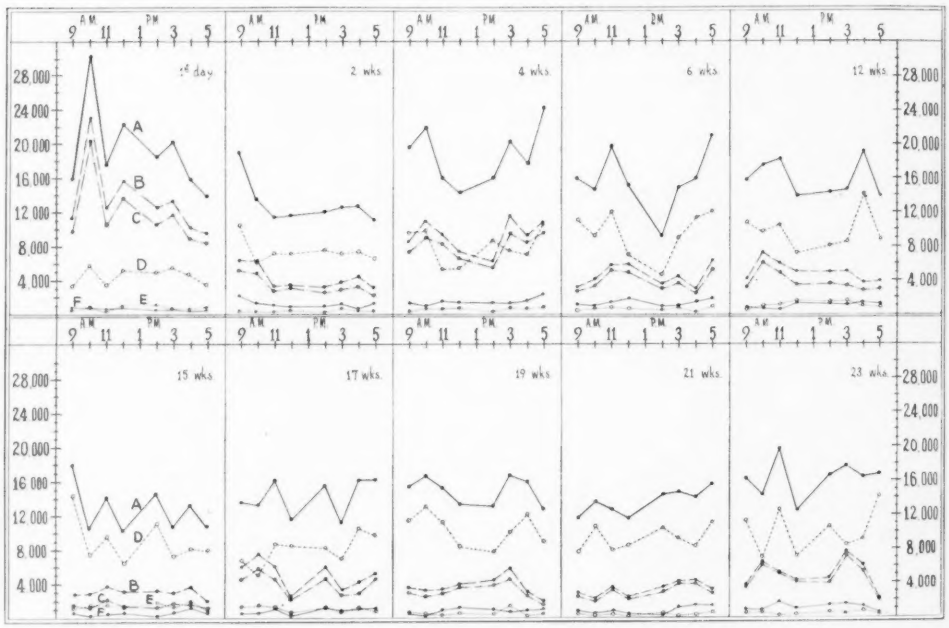

Fig. 4.—Curves depicting the hourly fluctuations of all the leukocyte counts on selected days between birth and the sixth month in case 19.

the new-born period in each is the usual one, with a high total leukocyte count combined with a marked preponderance of the granulocyte group the curve for which parallels that of the total count as it does in the adult. Sharp rises and equally sharp drops in these two curves are apt to occur at any hour, but in the observations during the new-born period recorded here they were noted most frequently in the morning hours between 9:00 and 11:00. The lymphocytes rarely show sudden fluctuations during the first ten days of life. The monocytes and eosinophils are also likely to maintain a more constant level. During the first two to six days the neutrophils show a rapid decline, the lymphocytes remain-

ing approximately at a level so that the decline in the curve for granular cells parallels that for the total number of white blood cells. This may be seen by comparing the curves for the first day and for the first week in figure 3.

Some time between the end of the first and the seventh week the lymphocytes become predominant. Figures 3 and 4 show correctly that this is not apt to be a sudden transition, as with the decrease in the polymorphonuclears, but is gradual and sometimes variable. Thus, in case 16 there was a slow but steady rise in the number of lymphocytes from the first to the fifth week, when they were overwhelmingly the dominant cell. Even in the record for the third week it can be seen that the fluctuations in the lymphocyte count determined the shape of the curve representing the total leukocyte counts. In contrast with this picture, there was a slower and less steady emerging of the lymphocytic preponderance in case 19 from the second to the sixth week. Moreover, the polymorphonuclears remained at a considerably higher level during this transition in case 19 than in case 16. The babies in both cases appeared to be equally healthy at this age, although it is of some interest to note that in case 19 the red blood cell content was maintained at from 5,000,000 to 5,500,000, whereas the red blood cell count in case 16 dropped to 4,000,000 at the thirteenth week without any added medication. This might be taken as evidence of greater activity in the bone marrow in the early weeks in case 19, which might in turn explain the higher percentage of bone marrow leukocytes.

From the end of the sixth or seventh week to the sixth month there were no further significant or constant changes. The majority of the sharp fluctuations in the lymphocyte counts are reflected in the curve of the total leukocyte counts. Occasionally this is not true, as, for instance, in the curves for the last day in figure 4, in which a sharp drop in the number of polymorphonuclears coincident with a rise in the number of lymphocytes resulted in a constant level for the total leukocyte curve. In the curves for the seventeenth week for the same case may be seen an instance of a sharp rise in the number of granulocytes, producing a parallel rise in the total count, while the lymphocyte count remained relatively stationary. In other words, the parallelism between the curves for the lymphocyte and total white blood cell counts is not such a constant phenomenon as to enable one to attach pathologic significance to occasional sharp rises in the neutrophils, even when such rises are associated with a coincident rise in the total count. In 8 of approximately 400 counts done between the eighth and the twenty-sixth weeks there were actually a larger number of granulocytes than of lymphocytes at some one hour during the day. There was some tendency for peaks of the granulocyte curves to occur either between 9:00 and 11:00 a. m. or between 3:00 and 5:00 p. m. or at both times, but this

was by no means a constant phenomenon. The curve of the monocyte counts shows little if any correspondence with any other curve. If it parallels any during a given day it is more apt to resemble that of the neutrophils than that of the lymphocytes.

Nine series of hourly counts during the night were carried out on five babies. Two of these series were part of a twenty-four hour period of hourly counts, skipping the hours of 8:00 a. m., 1:00 p. m., 6:00 p. m. and 1:00 a. m. One of these is depicted in figure 3 for a baby aged 13 weeks. This particular set of curves might lead one to suspect the existence of a twelve hour rhythm, but the remaining series of counts taken at night did not bear out any such thesis. All nine of the series of counts done during the night showed approximately the same type and extent of variations as those done during the day. That the baby in case 16 should have had his highest leukocyte count at 3:00 a. m. is one of the many findings which are hard to explain. At present I am concerned with building up the picture of what variations may be found during good health without regard to their physiologic cause. It may be of interest to note, however, that the baby in case 16 was asleep from 2:00 until 6:00 a. m. except for partial arousing for the hourly counts and the taking of his temperature, which remained below 99 F. during this period. The results of the hourly counts during the night certainly suggest that the blood of an infant does not show any so-called basal leukocyte level. In a recent article Sweizer [4] reported his inability to demonstrate the existence of a basal leukocyte level in young adults. Whether there is any such phenomenon at any age seems doubtful, but at any rate no correlation has been noted in this study between the degree of activity and the fluctuations of the count of any of the leukocytes.

A study of figures 3 and 4 together with the data contained in tables 1 and 2 should give a fairly complete picture of the variations in the differential counts of healthy infants during the first six months of life. Although the total leukocyte counts for these seven babies have been presented, the picture may be brought out more clearly if all the 908 total counts on the twenty babies are summarized as a final report on the variations in the total white blood cell count during the first six months.

FINAL REPORT ON 908 TOTAL LEUKOCYTE COUNTS

In figure 5 all the 908 leukocyte counts on twenty babies are scattered according to the exact day of age. Subsequent to the new-born period the variation was from 5,000 to 24,150. This is so tremendous a range that it makes one hesitate to call it the zone of normal health, even

4. Sweizer, M.: Basal Level of Leukocytes in Man, Am. J. Physiol. **105**:217 (July) 1933.

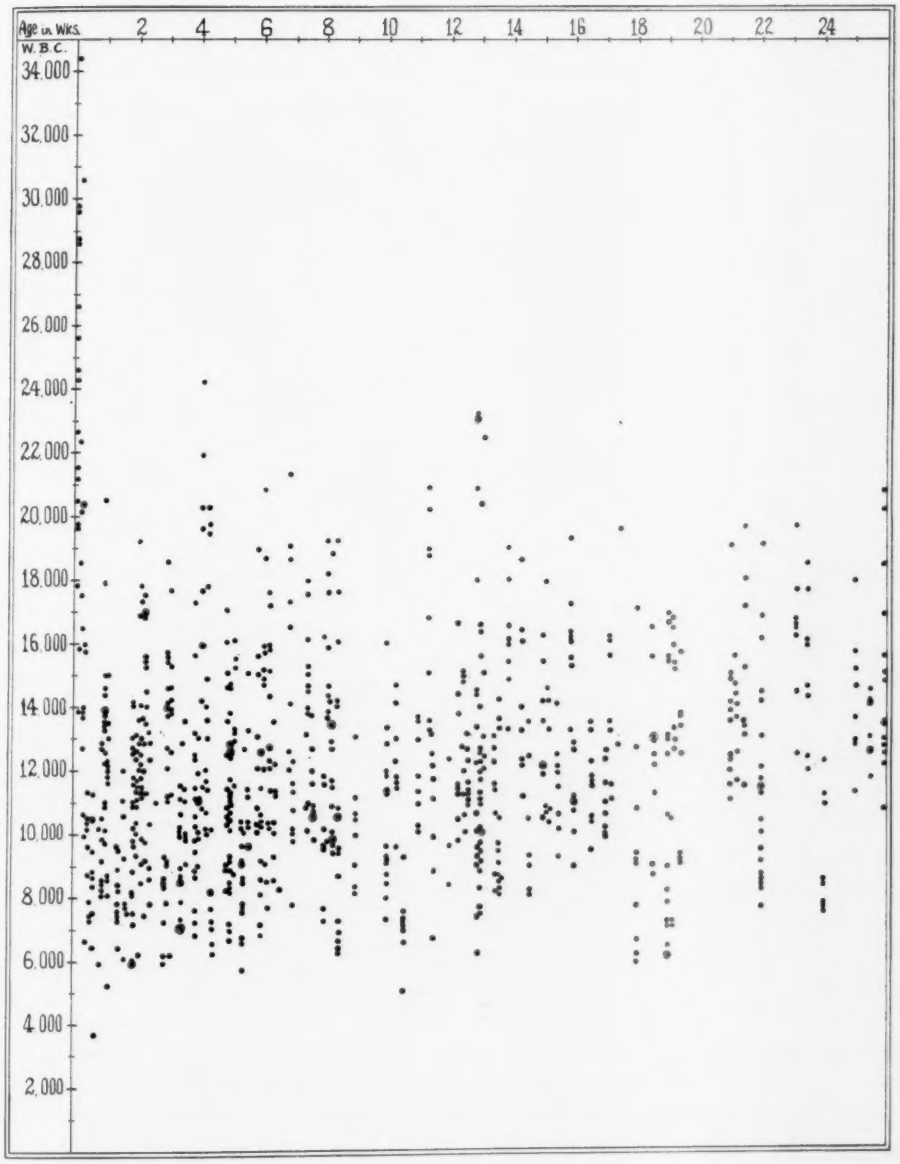

Fig. 5.—A graph of 908 total leukocyte counts on twenty babies, scattered according to the day of age from birth to 26 weeks.

though these infants were followed carefully and were always checked for any evidence of disease whenever the counts showed some unusual trend. If one takes off 10 per cent of the counts from both the top and the bottom of the zone on the assumption that the middle 80 per cent would represent more safely a zone of average health, one would have a range from 8,000 to 16,500. If these 908 counts were on nine hundred and eight different babies such a procedure might be justified on a

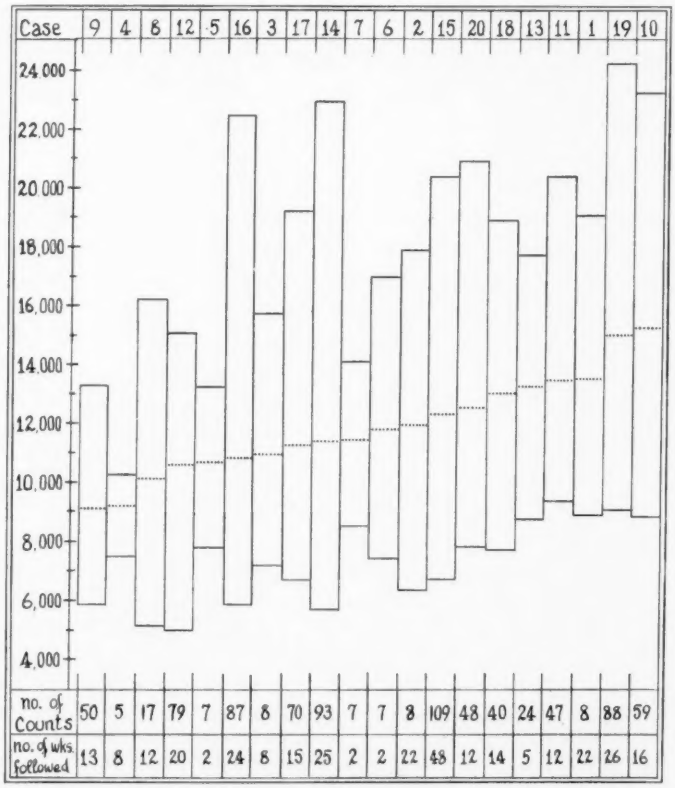

Fig. 6.—Comparison of the ranges of variation in the total leukocyte counts of twenty babies between the second and twenty-sixth weeks of life. The average of all the counts in each case is indicated by a dotted line, the cases having been arranged in the ascending order of these averages. At the foot of the chart are indicated the number of counts performed for each case and the number of weeks during which the counts were made.

statistical basis. But this was a small group of infants who had been watched with care from the time of birth throughout the period covered by the counts without showing observable evidence of disease. From the practical clinical point of view the important fact is that the number of leukocytes may rise to 20,000 or drop to 5,000 in an apparently

healthy baby who has not shown any evidence of previous infection and who shows no such evidence in the follow-up period.

The zones within which the total leukocyte counts varied in each of the twenty infants from the second to the twenty-sixth week are compared in figure 6. The average of all the counts in each case is indicated by a dotted line, the cases having been arranged in the ascending order of these averages. At the foot of the figure are shown the number of counts performed in each case and the number of weeks during which the counts were made. Some correlation may be noted between the extent of the range and the number of counts done, although this is not as constant as one might expect. In case 9, with 50 counts, the range was smaller than in case 6, with 7 counts, while in case 12, with 79 counts, the range was the same as in case 1, with 8 counts. Nor is there a very close relationship between the extent of the range and the length of the follow-up period. Thus, in case 12, in which a large number of counts was made over a period of twenty weeks, the range was considerably smaller than that in case 20, in which counts were made for only twelve weeks. However, it is true that over 80 counts were made on the three babies whose counts showed the greatest range of variation, and all these babies were followed up for six months. An erroneous picture of the extent of the range in a given baby may be obtained in too short a follow-up period. The most extreme example of this may be seen by comparing the range noted in the counts of case 14 in the first paper [1] of this series (from 5,900 to 13,500) with that noted for the same infant in figure 6, in which 43 more counts covering a period of four more months increased the range to from 5,700 to 22,900.

In the summary of the previous report there appeared the statement that "the leukocyte counts in any individual baby tend to fluctuate within a definite zone, but this zone is not the same for every baby of a given size or age." Even though there is some tendency toward a minimizing of these differences when a large number of counts are done over the whole six month period, yet the comparison of zones in figure 6 still bears out the truth of this statement. A comparison of the average for each group of counts gives an even more striking example of the individual differences. Thus, in the two cases (14 and 16) in which the zones of fluctuation were widest the averages were 11,300 and 10,700, as compared with the average figures of 14,900 and 15,100 for the next two cases, in the order of the extent of the range. In case 18, with 40 counts and a follow-up period of fourteen weeks, there was a relatively small range but the relatively high average of 13,000. It would appear that the additional material contained in this final report on the total leukocyte counts does little more than bring out more clearly and conclusively the picture of individual variations in the white blood cell counts of healthy infants.

SUMMARY AND CONCLUSIONS

The results of 908 total leukocyte counts on twenty healthy infants together with an analysis of 608 differential counts on seven of these infants are presented by means of tables and charts.

The majority (800) of these counts were done between the hours of 9:00 a. m. and 5:00 p. m., the remainder being done during the night. In most instances 8 counts were made in one day, from six to twelve such series being done on each baby during the first three to six months of life.

Concerning the leukocyte counts of the blood of healthy infants from the second to the twenty-sixth week of life the following conclusions seem justified:

1. The total leukocyte count may vary from 5,000 to 24,000 without indicating the presence of demonstrable disease, but the majority of the counts (the middle 80 per cent) lie between 8,000 and 16,500.

2. Fluctuations in the counts of all the white blood cells during the hours of the day and night show no tendency to orderly rhythm, vary a great deal from one day to another and show no correlation with age, activity, feedings or the routine events of the day.

3. The curve of the lymphocyte counts is the only one which shows a persistent tendency to parallel that of the total leukocyte counts.

4. The limits of variation which may be expected in each of the main groups of leukocytes are approximately as follows: lymphocytes, from 2,300 to 15,700 per cubic millimeter (from 27 to 88 per cent); polymorphonuclear neutrophils, from 500 to 9,500 (from 5 to 63 per cent); all the granulocytes, from 650 to 11,500 (from 10 to 68 per cent), and monocytes, from 150 to 2,400 (from 1 to 18 per cent).

5. The variation in the differential leukocyte counts of individual infants or in any one infant from time to time is as striking as that previously reported in the total leukocyte counts.

Case Reports

MINERAL METABOLISM

A CASE OF OSTEOPSATHYROSIS AND ONE OF UNUNITED FRACTURE

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DETROIT

The patients on whom these studies were made were admitted to the Children's Hospital at about the same time, and as they presented difficult but not uncommon clinical problems, it was decided to make as complete an investigation as possible of their mineral metabolism. The study did not bring out anything of definite assistance in the handling of the cases, but gave some interesting observations. These are reported in detail, because complete studies on the mineral metabolism of children are rare, and it seems desirable to have them on record.

REPORT OF CASES

CASE 1.—*Osteopsathyrosis.*[1]

History.—M. F., a girl of 11 years, was admitted for study in November 1931, because of frequent fractures from slight cause and marked increasing scoliosis, for which she was receiving orthopedic treatment from one of the members of the staff.

The family history was irrelevant, and there had been nothing of note in the patient's first year of life, except that cereals and vegetables were given

From the Research Laboratory, Children's Fund of Michigan, and the Children's Hospital of Michigan.

A preliminary report of this study was read before the American Society of Biological Chemists at the meeting of the Federation of American Societies for Experimental Biology, Philadelphia, April 29, 1932 (Hunscher, H. A.; Cope, F.; Noll, A.; Macy, I. G.; Cooley, T. B.; Penberthy, G. C., and Armstrong, L.: Successive Mineral Balances in Childhood, J. Biol. Chem. **97**:lxiv, 1932).

1. This name is used not in the sense of an exact diagnosis but because it comes as near to describing the condition as does any term in the rather vague classification of the disorders of bone.

rather late and that she had received no cod liver oil, though orange juice was given. There was no history of the ordinary symptoms of rickets. She walked at the age of 16 months.

She had measles, mumps and chickenpox in early childhood, but was not subject to coughs, colds or sore throat. She had occasional nosebleed and always had noticeably cold hands. The sclerae were blue and there were dark circles under the eyes.

The patient had had five fractures, all below the knees. The first occurred at the age of about 13 months, for no definite cause; the second, at 2 years, followed an effort to stand on tiptoe; the third occurred on a slight fall on a slippery sidewalk, and the fourth happened with a slip on the kitchen floor. After the third fracture she received treatment for rickets, including cod liver oil and therapy from a quartz mercury vapor arc lamp. After the fourth fracture she wore braces for a long time and had no more fractures until the summer of 1930, when she turned an ankle on the sidewalk and fractured the left tibia, which resulted in a shortening of about ½ inch (1.2 cm.). Healing occurred in a normal time after each fracture.

The scoliosis was first noticed in June 1931. She had seemed well up to that time. The deformity increased rapidly. She grew considerably in height during the year preceding admission to the hospital.

Physical Examination.—The patient was a pleasant-tempered, bright-appearing child. She was moderately well grown and slender, with good musculature and little fat. Her coloring was brunette, and her hair was black, rather coarse and dry. Her skin was clear and of normal texture and moisture. There was a large pigmented mole just below and to the left of the navel. The sclerae were definitely blue.

The head was well shaped and dolichocephalic. The eyes and ears were normal. The tonsils were small and not obviously diseased.

The neck was normal. There was no palpable goiter or parathyroid bodies and no adenoid swellings.

The thorax showed marked scoliosis involving the whole dorsal segment of the spine, with the convexity to the right and a corresponding deformity of the ribs.

The heart, lungs and abdomen were normal.

There were no deformities of the arms or legs. No callus was felt on the bones of the legs except one small lump at the junction of the middle and lower thirds of the left tibia. The measurement from the anterior superior spine of the ilium to the external malleolus on the right was 76 cm. and on the left, 75 cm.

There were no glandular enlargements.

The neurologic examination gave negative results.

The metabolic rate was — 5 per cent.

The blood count showed: red cells, 4,140,000, and of normal size, shape and staining reactions; hemoglobin content (Sahli), 80 per cent; white cells, 8,200; polymorphonuclears, 58 per cent; large lymphocytes, 17 per cent; small lymphocytes, 20 per cent; monocytes, 3 per cent; eosinophils, 1 per cent; platelets, 300,000 and volume of corpuscles, from 49.4 to 50 per cent. A chemical study of the blood showed: total serum calcium, 11.85 mg.; phosphorus, 2.06 mg., and cholesterol, 106.9 mg. per hundred cubic centimeters of blood.

Roentgen Examination.—Films had been made of practically the whole skeleton in April and in July 1931. These showed normal epiphyseal development everywhere and good general development of the bones. There seemed to be slightly less than the normal calcium content of all the bones; the decrease was most

noticeable in the ribs, in which some slight cystic changes, not of the type seen in parathyroid disturbance, were observed in the first films. Trabeculation seemed normal.

There was marked scoliosis, with dorsal convexity to the right and lumbar convexity to the left. No destruction of any vertebrae was seen (fig. 1).

The bones of the legs showed no abnormalities except slight scars of healed fractures in the left tibia and in the proximal phalanx of the fourth toe, with no displacement (fig. 2).

Fig. 1 (case 1).—Scoliosis, with no evidence of destruction of the vertebrae.

Dental Examination.—Hypoplasia of the permanent teeth, some rough and improperly formed enamel, a few areas of defective calcification and twelve carious permanent teeth were revealed.

Psychologic Examination.—The child was above the average in intelligence and of normal behavior except for the suggestion of nervous strain given by closely bitten finger-nails.

CASE 2.—*Ununited Fracture.*

History.—D. B., a girl of 7½ years, was admitted to the hospital in September 1931 because of ununited fractures of the right tibia.

The family history was wholly irrelevant. The child had apparently been a normal baby, breast fed for eight months and then given a dried milk preparation.

She had no cod liver oil until the age of 18 months, but received plenty of sunlight. She seemed to develop normally until it was noticed that she showed no inclination to walk at the ordinary time, and bowing of the right tibia was observed, for which the family physician applied an apparatus with no effect. When at the age of 2 years she did not walk, an orthopedic surgeon diagnosed severe rachitic deformity and performed an osteotomy. Some months later the fracture was found not to have healed, and an inlay of bone was inserted. She remained in the hospital for a year, receiving treatment with sunlight, massage and

Fig. 2 (case 1).—Slight scars of healed fractures in the left tibia.

cod liver oil. She then had a variety of treatments in a number of clinics, including various diets, apparatus, physical therapy and four bone grafting operations. At times there seemed to be slight union, which always broke down. Following one of the operations, hemiplegia developed, which was supposed to be due to fat embolism. Recovery from this was complete after several months, but in the meantime the child became left-handed. When she was admitted to the Children's Hospital she was wearing a brace, by means of which she got around fairly well.

Physical Examination.—D. B. was a bright, well behaved child. She was plump and well developed, with blond coloring and brown hair and a clear skin of good color and texture. The sclerae were normal.

The head was well shaped. The eyes and the ears were normal. The tonsils were of medium size and were moderately diseased. There was considerable lymphoid hyperplasia on the posterior pharyngeal wall. The neck was normal.

The thorax was well developed, with no deformity. The lungs were normal. The heart area and heart rate were normal. There was a soft systolic murmur which was not transmitted. The abdomen was normal.

The arms and thighs were normal. A brace was worn on the right leg. Both legs showed scars of old operations. There was approximately a 3 cm. shortening of the right leg.

Fig. 3 (case 2).—A slight increase can be seen in the amount of callus about the fractures, but the segments are not firmly united.

The neurologic examination gave normal results.

The blood count showed: red cells, 4,610,000, of normal size, shape and staining reactions; hemoglobin content (Sahli), 85 per cent; white cells, 5,800; polymorphonuclears, 40 per cent; large lymphocytes, 18 per cent; small lymphocytes, 32 per cent; monocytes, 1 per cent; basophils, 1 per cent; eosinophils, 8 per cent; platelets, 300,000, and volume of corpuscles, from 46.4 to 47 per cent.

The chemical study of the blood showed the total serum calcium, phosphorus and cholesterol to be 12.15, 2.14 and 97 mg., respectively, per hundred cubic centimeters of blood.

Roentgen Examination.—On Sept. 10, 1931, films were made of both legs in two planes; of the forearms and arms in the anteroposterior plane; of the skull in the right and left lateral projections, and of the pelvis and the regions of both thighs in the anteroposterior projection.

The films demonstrated ununited fractures through the shaft of the tibia in the middle third. The fragments were in end-to-end contact, but there was slight lateral angulation at the points of fracture. There was considerable diminution in the diameter of both the tibia and the fibula of the left leg. Both the bones showed definite loss of lime substance, and there were transverse striations through the diaphyseal ends which we interpreted as indicating so-called growth lines. Similar lines were demonstrated in the films of the forearms. There was no apparent disturbance in the normal epiphyseal development.

The film of the right leg showed some thickening of the cortex of the tibia with slight periosteal roughening but no changes to suggest a definite destructive disease.

The films of the skull revealed no unusual changes in the contour or detail of the cranial vault.

On Sept. 9, 1933, additional study was made of the left leg. There was a slight increase in the amount of callus about the fractures, but the segments were not firmly united (fig. 3).

Examination of the Legs.—There was atrophy of the right leg, with some apparent shortening. The distance from the umbilicus to the internal malleolus on the right measured 31 inches (78.7 cm.) and on the left, 32 inches (81.2 cm.). The distance from umbilicus to the inferior border of the patella was 18½ inches (47 cm.) on both the right and the left. There were scars on the anterior aspect of both the left and the right leg, the result of operations. There were good flexion and extension at the right knee and ankle. There was some lateral bowing of the middle third of the right leg as well as false motion of the middle third of the right tibia. The fibula was intact.

Dental Examination.—Caries was present in eight deciduous and four permanent teeth, and there was nonunion of the sulci in the six year molars. There was evidence of hypoplasia in both the deciduous and the permanent teeth, and there were some areas of imperfect calcification. Dr. Charles Bodecker, professor of oral histology and embryology at Columbia University, examined an extracted molar and reported poor calcification of both the enamel and the dentin, with resorption at the margins of the pulp canals followed by the formation of osteoid tissue, indicating the activity of a pathologic process in the pulp.

Psychologic Examination.—The child had a rather low average of general intelligence. She had been somewhat overprotected. There was, however, nothing of special significance.

STUDIES ON METABOLIC BALANCE

The two girls of this study, 7½ and 11 years of age and weighing approximately 23 and 30 Kg., respectively, were maintained on a constant intake of food under identical experimental conditions, and the nitrogen, calcium, magnesium, potassium, sodium, phosphorus, sulphur and chlorine and, subsequently, the total acid-base mineral balances were determined over four or five successive five day periods. The amounts of the basic elements (sodium, potassium, calcium and magnesium) and the acid elements (chlorine, sulphur and phosphorus), as well as

the nitrogen content, were determined in the food, urine and feces, respectively, by standard methods of analysis,[2] and for direct comparison the amount of each substance was calculated in terms of chemical equivalents of normal acid or alkali. Chlorine, sodium and potassium were computed as monovalent, calcium, magnesium and sulphur as divalent, and phosphorus as 1.8.[3]

The mineral content of the diet was kept constant, identical amounts of the same foods being served each day in frequently varied menus. The basal diet was made up of the following quantities of foodstuffs in grams per day: apple, 100; banana, 100; beef, 100; white bread, 60; whole wheat bread, 30; cabbage or carrot, 50; celery, 20; American cheese, 15; egg, 50; lettuce, 20; milk, 400; orange, 100; potato, 70; shredded wheat or farina, 30; tomato, 60, and filtered butter, 30. This diet yielded 1,720 calories, 60 Gm. of protein, 0.8 Gm. of calcium, 1.04 Gm. of phosphorus, 0.34 Gm. of magnesium, 1.5 Gm. of sodium, 3.95 Gm. of potassium, 0.66 Gm. of sulphur and 3.05 Gm. of chlorine daily. If the appetite of the child was not completely satisfied, sugar and pure stick candy were given in known quantities. Distilled water was taken ad libitum.

There was retention of calcium, magnesium, potassium, phosphorus, sulphur and nitrogen (fig. 4 and tables 1 and 2). The balances for sodium and chlorine, which were negative in the first period of adjustment, later became positive. In a recent report[4] it was pointed out

2. The following methods were used: for sodium, that of Butler and Tuthill (Butler, A. M., and Tuthill, Elizabeth: An Application of the Uranyl Zinc Acetate Method for Determination of Sodium in Biological Material, J. Biol. Chem. **93**: 171, 1931); for potassium, that of Kramer and Tisdall (Kramer, B., and Tisdall, F. F.: Methods for the Direct Quantitative Determination of Sodium, Potassium, Calcium, and Magnesium in Urine and Stools, ibid. **48**:1, 1921); for calcium and magnesium, that of McCrudden (McCrudden, F. H.: The Quantitative Separation of Calcium and Magnesium in the Presence of Phosphates and Small Amounts of Iron Devised Especially for the Analysis of Foods, Urine, and Feces, ibid. **7**: 83, 1910; The Determination of Calcium in the Presence of Magnesium and Phosphates: The Determination of Calcium in Urine, ibid. **10**:187, 1911); for chlorine, that of Volhard and Arnold (cited by Hawk and Bergeim: Practical Physiological Chemistry, ed. 10, p. 879); for sulphur, that of Benedict (Benedict, S. R.: The Estimation of Total Sulphur in Urine, J. Biol. Chem. **6**:363, 1909); for phosphorus, that of Youngburg (Youngburg, G.: The Partition of Phosphorus in Blood, J. Lab. & Clin. Med. **16**:158, 1930), and for nitrogen, that of Kjeldahl.

3. Shohl, A. T.: Mineral Metabolism in Relation to Acid-Base Equilibrium, Physiol. Rev. **3**:509, 1923. Shohl investigated acid-base balances emanating from the metabolism of certain mineral substances. The acid values and base values of the elements were designated as valences. The values for these valences sometimes are, and sometimes are not, identical with chemical valences. The values are physiologic factors and are not to be confused with chemical valences.

4. Unpublished data reported before the Division of Medicinal Chemistry at the Eighty-Sixth Annual Meeting of the American Chemical Society, Chicago, Sept. 14, 1933.

that it may take a month or more for a healthy child to become adjusted to a given intake of potassium, and that this element in turn may affect the utilization of sodium and chlorine. The negative balances for sodium and chlorine no doubt represented an adjustment of the body to the basal diet, which is in agreement with similar observations recently reported by Wiley, Wiley and Waller.[5] It is interesting to note (tables 1 and 2) that although the excretion of calcium in the urine was different for the two children of the present study it fell within the normal range.

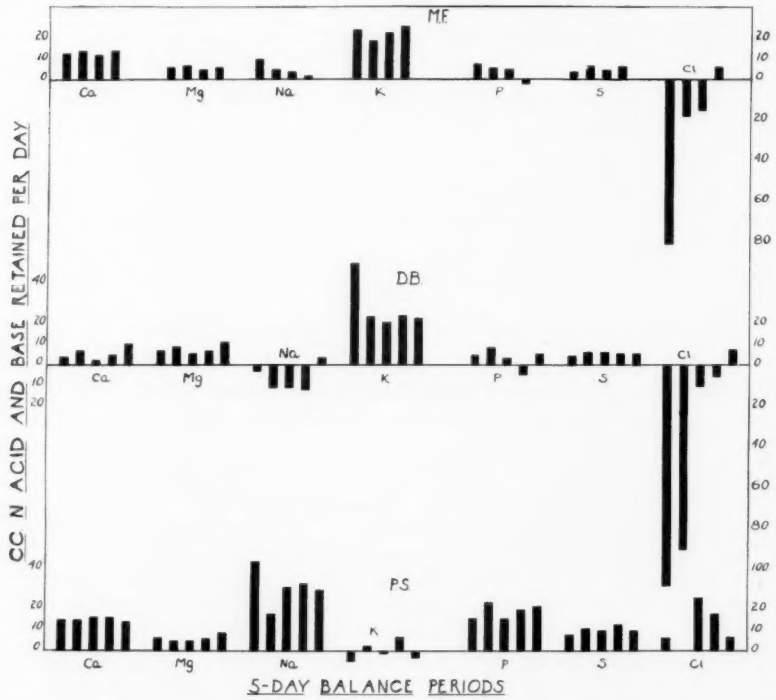

Fig. 4.—The retention of the basic and acid elements for the two experimental subjects, M. F. and D. B., and for the normal control, P. S. As a means of direct comparison, the data are shown in terms of cubic centimeters of normal acid and base.

Calcium was stored at different rates by the two subjects under consideration. The calcium retention for M. F. was approximately twice as high as that for D. B. under identical experimental and dietary conditions, and in neither was the calcium and phosphorus retention as high

5. Wiley, F. H.; Wiley, L. L., and Waller, D. S.: The Effect of the Ingestion of Sodium, Potassium, and Ammonium Chlorides and Sodium Bicarbonate on the Metabolism of Inorganic Salts and Water, J. Biol. Chem. **101**:73, 1933.

as that for the normal child used as a control (chart 1).[6] Boyd, Drain and Stearns [7] recently showed that there is a relationship between the amount of calcium customarily retained by a child and the occurrence of dental caries. Both of our subjects had many teeth with cavities,

TABLE 1.—*Daily Metabolic Balances of M. F.*

Period No.	Body Weight, Kg.	Total Exchange				Per Kg. of Body Weight		Path of Outgo		
		Intake, Gm.	Urine, Gm.	Feces, Gm.	Retention, Gm.	Intake, Gm.	Retention, Gm.	Urine, per Cent	Feces, per Cent	Retention, per Cent
Nitrogen										
1	31.0	9.73	8.41	0.99	+0.33	0.314	+0.011	86.4	10.2	3.4
2	30.6	9.73	8.17	0.77	+0.80	0.318	+0.026	83.9	7.9	8.2
3	30.4	9.73	8.19	0.71	+0.83	0.320	+0.027	84.1	7.3	8.6
4	30.3	9.73	8.36	0.90	+0.48	0.321	+0.016	85.9	9.2	4.9
Phosphorus										
1	31.0	1.04	0.47	0.42	+0.14	0.0334	+0.0046	45.2	40.9	13.8
2	30.6	1.04	0.60	0.33	+0.10	0.0339	+0.0032	58.4	32.1	9.5
3	30.4	1.04	0.62	0.33	+0.10	0.0341	+0.0031	59.4	31.4	9.1
4	30.3	1.04	0.71	0.36	—0.03	0.0342	—0.0010	68.2	34.9	...
Calcium										
1	31.0	0.80	0.06	0.48	+0.26	0.0257	+0.0084	7.4	59.7	32.8
2	30.6	0.80	0.07	0.45	+0.28	0.0261	+0.0091	9.0	56.2	34.8
3	30.4	0.80	0.06	0.49	+0.25	0.0262	+0.0082	7.6	61.1	31.3
4	30.3	0.80	0.05	0.47	+0.28	0.0263	+0.0091	5.7	59.5	34.8
Magnesium										
1	31.0	0.34	0.10	0.18	+0.07	0.0111	+0.0022	28.8	51.6	19.7
2	30.6	0.34	0.10	0.16	+0.08	0.0112	+0.0028	28.9	46.5	24.6
3	30.4	0.34	0.12	0.16	+0.06	0.0113	+0.0019	35.9	47.3	16.9
4	30.3	0.34	0.11	0.17	+0.07	0.0113	+0.0023	31.2	48.9	20.0
Sodium										
1	31.0	1.47	1.21	0.03	+0.23	0.0474	+0.0074	82.2	2.2	15.6
2	30.6	1.55	1.41	0.03	+0.11	0.0505	+0.0035	91.2	1.9	6.9
3	30.4	1.39	1.27	0.02	+0.10	0.0457	+0.0032	91.2	1.8	7.0
4	30.3	1.55	1.48	0.02	+0.05	0.0510	+0.0017	95.7	1.0	3.3
Potassium										
1	31.0	3.95	2.58	0.44	+0.93	0.1273	+0.0300	65.3	11.1	23.6
2	30.6	3.95	2.90	0.30	+0.74	0.1290	+0.0242	73.5	7.7	18.7
3	30.4	3.95	2.70	0.34	+0.91	0.1298	+0.0298	68.5	8.6	23.0
4	30.3	3.95	2.59	0.33	+1.02	0.1302	+0.0338	65.6	8.4	26.0
Sulphur										
1	31.0	0.66	0.51	0.09	+0.06	0.0214	+0.0020	76.8	14.1	9.2
2	30.6	0.66	0.50	0.05	+0.11	0.0216	+0.0037	75.2	7.6	17.1
3	30.4	0.66	0.52	0.07	+0.08	0.0218	+0.0025	78.3	10.3	11.4
4	30.3	0.66	0.50	0.06	+0.11	0.0219	+0.0036	75.0	8.4	16.6
Chlorine										
1	31.0	3.02	5.81	0.04	—2.83	0.0973	—0.0913	192.4	1.4	...
2	30.6	3.14	3.74	0.04	—0.65	0.1026	—0.0211	119.2	1.4	...
3	30.4	2.90	3.41	0.03	—0.54	0.0953	—0.0179	117.9	0.9	...
4	30.3	3.14	2.88	0.02	+0.24	0.1036	+0.0078	91.8	0.7	7.5

and the teeth were poorly formed, both of which conditions corroborated the observations of Boyd, Drain and Stearns.

6. Data on the acid-base mineral balances of normal children are to be reported later.

7. Boyd, J. D.; Drain, C. L., and Stearns, G.: Metabolic Studies of Children with Dental Caries, J. Biol. Chem. **103**:327, 1933.

An interesting observation on both the children was that though the mothers indicated that they had received liberal, sensible diets at home, preliminary study showed that neither ate well. M. F. was not

TABLE 2.—*Daily Metabolic Balances of D. B.*

Period No.	Body Weight, Kg.	Total Exchange				Per Kg. of Body Weight		Path of Outgo		
		Intake, Gm.	Urine, Gm.	Feces, Gm.	Retention, Gm.	Intake, Gm.	Retention, Gm.	Urine, per Cent	Feces, per Cent	Retention, per Cent
Nitrogen										
1	23.5	9.73	7.99	0.79	+0.95	0.414	+0.040	82.1	8.2	9.7
2	23.5	9.73	7.68	0.75	+1.31	0.414	+0.056	78.9	7.7	13.4
3	23.5	9.73	7.56	0.81	+1.36	0.414	+0.058	77.7	8.4	13.9
4	23.6	9.73	8.15	0.94	+0.64	0.412	+0.027	83.7	9.7	6.6
5	23.7	9.73	8.37	0.84	+0.52	0.411	+0.022	86.0	8.6	5.3
Phosphorus										
1	23.5	1.04	0.54	0.42	+0.08	0.0441	+0.0034	51.6	40.7	7.6
2	23.5	1.04	0.44	0.45	+0.15	0.0441	+0.0064	42.1	43.4	14.5
3	23.5	1.04	0.55	0.42	+0.06	0.0441	+0.0027	53.0	40.9	6.1
4	23.6	1.04	0.67	0.44	−0.08	0.0439	−0.0033	64.9	42.5	...
5	23.7	1.04	0.61	0.32	+0.10	0.0437	+0.0044	58.5	31.4	10.1
Calcium										
1	23.5	0.80	0.13	0.59	+0.07	0.0339	+0.0031	16.7	74.1	9.2
2	23.5	0.80	0.10	0.55	+0.14	0.0339	+0.0060	13.1	69.3	17.6
3	23.5	0.80	0.09	0.67	+0.03	0.0339	+0.0013	11.8	84.1	4.0
4	23.6	0.80	0.06	0.64	+0.10	0.0338	+0.0040	7.9	80.1	12.0
5	23.7	0.80	0.06	0.54	+0.19	0.0336	+0.0081	7.9	68.0	24.1
Magnesium										
1	23.5	0.343	0.116	0.142	+0.086	0.0146	+0.0036	33.7	41.4	24.9
2	23.5	0.343	0.088	0.145	+0.110	0.0146	+0.0047	25.5	42.3	32.2
3	23.5	0.343	0.099	0.171	+0.073	0.0146	+0.0031	28.8	49.9	21.3
4	23.6	0.343	0.101	0.160	+0.082	0.0145	+0.0034	29.5	46.7	23.8
5	23.7	0.343	0.089	0.115	+0.139	0.0145	+0.0058	25.9	33.6	40.4
Sodium										
1	23.5	1.15	1.23	0.01	−0.09	0.0491	−0.0037	106.6	1.0	...
2	23.5	1.15	1.40	0.01	−0.25	0.0491	−0.0108	121.2	0.8	...
3	23.5	1.07	1.30	0.01	−0.24	0.0457	−0.0103	121.5	1.1	...
4	23.6	1.07	1.34	0.01	−0.28	0.0455	−0.0117	124.6	1.0	...
5	23.7	1.07	0.98	0.01	+0.08	0.0453	+0.0036	91.2	0.9	7.8
Potassium										
1	23.5	3.95	1.60	0.38	+1.96	0.1679	+0.0836	40.5	9.8	49.8
2	23.5	3.95	2.76	0.24	+0.95	0.1679	+0.0403	70.0	6.0	24.0
3	23.5	3.95	2.89	0.24	+0.81	0.1679	+0.0346	73.3	6.1	20.6
4	23.6	3.95	2.62	0.36	+0.96	0.1672	+0.0406	66.4	9.3	24.3
5	23.7	3.95	2.72	0.32	+0.91	0.1665	+0.0384	68.9	8.0	23.0
Sulphur										
1	23.5	0.662	0.512	0.072	+0.078	0.0282	+0.0033	77.4	11.0	11.7
2	23.5	0.662	0.500	0.061	+0.102	0.0282	+0.0043	75.4	9.2	15.4
3	23.5	0.662	0.493	0.070	+0.099	0.0282	+0.0042	74.5	10.6	15.0
4	23.6	0.662	0.511	0.053	+0.098	0.0281	+0.0042	77.2	8.0	14.8
5	23.7	0.662	0.509	0.059	+0.095	0.0279	+0.0040	76.8	8.9	14.3
Chlorine										
1	23.5	2.53	6.34	0.02	−3.83	0.1077	−0.1629	250.4	0.8	....
2	23.5	2.53	5.70	0.02	−3.20	0.1077	−0.1360	225.3	1.0	....
3	23.5	2.41	2.74	0.02	−0.36	0.1026	−0.0151	113.7	1.0	....
4	23.6	2.41	2.56	0.02	−0.16	0.1022	−0.0070	106.2	0.7	....
5	23.7	2.41	2.09	0.03	+0.29	0.1017	+0.0124	86.7	1.1	12.2

in the habit of eating a sufficient allowance of lime-containing foods, and D. B. consumed liberal quantities of milk but little other food.

Positive base retentions were found in all nine acid-base mineral balances for the two children (table 3). The data on the initial periods

demonstrate the marked adjustment to the experimental diet, followed by more nearly constant retention. The results during the last three periods are comparable with those reported in the literature for growing children. Shohl [3] showed that infants under 1 year of age retain 10 cc. ± 2 cc. of tenth-normal base per kilogram per day. Moreover, Sawyer, Baumann and Stevens [8] reported a positive base retention of 10 cc. and 14.5 cc. of tenth-normal alkali per kilogram per day for two boys, aged 5 and 8 years, weighing 22.7 and 23 Kg., respectively.

SUMMARY

There are some striking variations from the normal in the retention of certain elements in both children, the significance of which cannot at present be definitely appraised. During the five consecutive five day tests of metabolic balance, the normal child used as a control and the experimental subjects, M. F. and D. B., showed, respectively, an average daily retention per kilogram of body weight of: 18.8, 20 and 40.6 mg. of nitrogen; 15.2, 2.5 and 2.7 mg. of phosphorus; 13.4, 8.7 and 4.5 mg. of calcium; 3.6, 2.3 and 4.1 mg. of magnesium; 32.2, 4 and —1.8 mg. of sodium; 0.4, 29.4 and 47.5 mg. of potassium, and 7.2, 3 and 4 mg. of sulphur. The control child showed a retention of 19 mg. of chlorine but for the two experimental subjects there was an extreme loss of chlorine during the first periods of adjustment with a slight retention during the last period.

TABLE 3.—*Daily Base Balances in Terms of Cubic Centimeters of Tenth-Normal Acid or Base*

Subject		Period 1	2	3	4	5
M. F.	Urine	+ 932*	+244	+270	+116	—
	Feces	— 194	—209	—235	—216	—
	Total output	+ 738	+ 35	+ 35	—100	—
	Food†	— 462	—462	—462	—462	—
	Positive base balance					
	Total	+1,200	+497	+497	+362	—
	Per Kg. of body weight	38.7	16.2	16.3	11.9	—
D. B.	Urine	+1,313	+736	— 36	+ 64	+ 32
	Feces	— 219	—153	—246	—256	—218
	Total output	+1,094	+583	—282	—192	—186
	Food†	— 462	—462	—462	—462	—462
	Positive base balance					
	Total	1,557	1,045	180	270	276
	Per Kg. of body weight	66.2	44.4	7.7	11.5	11.7

* Plus shows an excess of acid and minus, an excess of base.
† The average daily intake of food contained 2,170 cc. of tenth-normal base and 1,708 cc. of tenth-normal acid, and gave an excess of 462 cc. of tenth-normal base per day.

8. Sawyer, M.; Baumann, L., and Stevens, F.: Studies in Acid Production: II. The Mineral Losses During Acidosis, J. Biol. Chem. **33**:103, 1918.

So far as definite clinical application of the findings in these two cases is concerned, the metabolic studies do not seem to justify a diagnosis of any of the classified disturbances of metabolism of bone.

Bion East, D.D.S., and Alberta Maloney Blakey, D.D.S., made the dental observations; Lawrence Reynolds, M.D., and E. R. Witwer, M.D., made the roentgen ray studies; Pearl Lee, M.D., made the blood study, and Margaret A. Rogers, R.N., Superintendent, Children's Hospital of Michigan, made this study in the hospital possible.

DIAPHRAGMATIC HERNIA ON THE RIGHT SIDE

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Cases of congenital hernia through the right side of the diaphragm in children in which life was spared for more than an hour are still sufficiently rare to be worthy of detailed report.

Greenwald and Steiner [1] made a careful review of the cases reported from 1912 through 1928, and of these only four from the English literature fall into this category. We have found in the subsequent English literature reports of only two definite cases of this type. The first case [2] was that of a 16 year old girl with a diaphragmatic hernia which roentgenographic studies showed to be "just lateral to the right border of the heart and situated anteriorly, and containing a segment of the proximal end of the transverse colon." The second case,[3] reported in 1933, occured in a boy of 2 months, whose hernia was ascribed to a failure of fusion of the pleuroperitoneal fold and the splanchnic mesoderm. Through the opening in the diaphragm passed almost the entire small intestine, the cecum and the ascending and the transverse colon.

Other cases in which the abdominal viscera lay in the right side of the chest were eliminated from this group for the following reasons: death in an hour or less after birth,[4] herniation apparently through the esophageal hiatus rather than through the diaphragm,[5] herniation through an aperture in the center of the diaphragm [6] and lack of detailed information.[7]

From the Radiological Service of Dr. Samuel F. Weitzner and the Pediatric Service of Dr. Louis H. Barenberg, Morrisania City Hospital.

1. Greenwald, H., and Steiner, M.: Diaphragmatic Hernia in Infancy and in Childhood, Am. J. Dis. Child. **38**:361 (Aug.) 1929.

2. Oliphant, T. H.: New Orleans M. & S. J. **83**:104 (Aug.) 1930.

3. Crumbie, G. R., and Stephens, J.: Brit. M. J. **2**:13 (July 1) 1933.

4. Smith, A. D.: M. J. Australia **2**:333 (Sept.6) 1930. Dodds, G. H., and Pocock, J. A.: Arch. Dis. Childhood **5**:233 (June) 1930. Chapman, E. F.: Brit. M. J. **2**:500 (Sept. 14) 1929. Dunne, G. P.: Minnesota Med. **10**:773 (Dec.) 1927.

5. Lightwood, R. C.: Proc. Roy. Soc. Med. **25**:783 (April) 1932.

6. Conybeare, J. J.; Donaldson, R., and Simpson, C. K.: Guy's Hosp. Rep. **82**:490 (Oct.) 1932.

7. Paterson, D.: Proc. Roy. Soc. Med. (Sect. Dis. Child.) **21**:1724 (Aug.) 1928. Brown, S.: J. Med. **11**:520 (Dec.) 1930.

EMBRYONIC DEVELOPMENT AND PATHOGENESIS

The development of the diaphragm is a complicated process. Early in fetal life there appears a semicircular shelf, the septum transversum, extending dorsad from the ventral portion of the body wall. On its superior aspect rests the heart, while fused to its inferior surface is the liver. This shelf only partially divides the coelom. The complete division into a pleural and a peritoneal portion is brought about by two pairs of folds which arise from the dorsolateral portions of the body wall—the pleuroperitoneal and pleuropericardial folds. These folds are roughly triangular, with their bases at the body wall and their apexes pointing toward the septum transversum, with which they eventually fuse.

At about the sixth week of embryonic life the openings between the peritoneal and pleural cavities close, and at about the same time muscle fibers begin to appear in the membranes which are forming the diaphragm. The last part of the diaphragm to close is the region at the site of the pleuroperitoneal canals, which are located in the dorsal wall of the body near the midline. Areas of muscular deficiency in the normal, fully developed diaphragm, called the foramina of Bochdalek, mark their position on both sides. Similar gaps in the muscle, called the foramina of Morgagni, through which pass the superior deep epigastric vessels, occur anteriorly on both sides of the sternum.

Congenital diaphragmatic hernia is considered as true or false depending on the presence of a sac. Such a sac indicates the formation of the hernia after development of the membranes which form the diaphragm.

Hernia develops as a result of failure of fusion of the component parts of the diaphragm, partial weakness in its structure which may possibly be the result of a localized pathologic condition or increased intra-abdominal pressure.

The various sites of diaphragmatic hernia are:

1. Through one of the foramina of Bochdalek (hiatus pleuroperitonealis).

2. Through the dome of the diaphragm as a result of an excessive degeneration of the muscle in the formation of the central tendon or of a local pathologic condition due to interference with the circulation or innervation.

3. Through the esophageal opening.

4. Through one of the foramina of Morgagni.

5. Through the gap left by the absence of the left half of the diaphragm, resulting from failure of development of the pleuroperitoneal membrane.

Various statistics have been cited to prove the relative frequency of diaphragmatic hernia on the left side as compared to that on the right side, but in general it may be stated that the ratio is about 7 : 1 or 10 : 1. The difference is explained by the later closure of the left side of the diaphragm, the poorer blood supply and the lack of the protection of the liver.

SYMPTOMS AND SIGNS

The symptoms are either gastro-intestinal or cardiorespiratory.

Gastro-intestinal symptoms may vary from none to those of complete obstruction. There may be frequent or occasional vomiting, relieved at times by holding the child in an upright position, and chronic or occasional constipation or diarrhea. Abdominal pain of great or moderate severity occurs at times, but this symptom is not frequent or valuable in the diagnosis of cases occurring in infancy or early childhood. All the symptoms vary with the amount and contents of the abdominal viscera in the thorax, the size of the aperture and the kinking which may be present. Difficulty in nursing and, in older children, inability to take food often occur, and because of these symptoms as well as of anorexia and vomiting there is often failure to gain weight.

The cardiorespiratory group of symptoms may be more prominent. At birth there may be feeble or convulsive respiration and subsequent bouts of dyspnea and hyperpnea and cyanosis. The cyanosis, like the vomiting, may be relieved by an upright position. Cough is a prominent symptom in many cases, and it also can be relieved by postural change. The cough is unproductive and usually paroxysmal.

The physical findings are bizarre, variable and inconstant. They depend on the amount and variety of viscera in the thorax and their contents at the time of examination. There may be bulging of the wall of the chest and diminution of the excursions of the chest on the affected side.

Displacement of the heart to the opposite side is common. Percussion reveals not only a shift in the position of the heart but extremely variable findings over the region of the herniated organs. Hollow viscera containing gas are tympanitic; those containing fluid give a dull or flat note, while solid viscera, such as the liver or spleen, have a flat sound on percussion. A full or partially full stomach may present dulness which shifts with the patient's position. Areas of tympany and of dulness may be present at the same time or at different times.

Auscultation reveals the change in cardiac location. Breath sounds vary from those of a normal quality to complete absence. They may be bronchial or amphoric. Râles may be audible not only over the region of the herniated organs but elsewhere in the chest. Intestinal rumbling or gurgling may be heard.

The variability of the physical findings in the chest is their most constant feature, and it is well to examine the patient at different intervals after eating and also on several days in order to demonstrate this fact.

The abdomen is often scaphoid, though strangulation may be followed by distention.

The diagnosis is rarely made clinically; indeed even to suspect it on the basis of the symptoms and physical findings is most unusual. Discovery of the condition is usually made on roentgenographic evidence, and its diagnosis during life is always clinched by this means.

REPORT OF A CASE

History.—A full term boy was born on April 27, 1934. The mother, aged 29, gave a history of no significance; the results of the physical examination and the Wassermann test of the blood were negative. Another pregnancy had occurred six years before, which had had a normal course. The child was living and well.

The patient weighed 6 pounds and 3 ounces (2,806.7 Gm.) at birth. The physical examination showed him to be normal. No cyanosis or other cardiorespiratory abnormality was noted.

For three days the child held his weight well, losing only 2 ounces (56.7 Gm.). Feedings from the breast were alternated with feedings from a bottle because of the mother's scanty supply. On May 1 the child vomited after the feedings and was jaundiced. The stools were dark. On the next day the vomiting continued, and the child refused the breast. The weight had fallen to 5 pounds (2,267.9 Gm.). Clyses of dextrose in saline solution were given. The next day vomiting ceased. Feedings were resumed, and the condition improved. On May 10, when the child was discharged from the hospital, the weight was 5 pounds and 6 ounces (2,438.1 Gm.).

On May 23 the mother brought the child to the clinic with a history of progressive loss of weight and cough for a few days. For one week he had been breast fed; after that he was given a complemental formula, which he vomited.

Examination.—Examination revealed a moderately dehydrated infant weighing 5 pounds and 3 ounces (2,353 Gm.). The significant physical findings were injection of the pharynx and right ear drum, a mucoid nasal discharge and flatness and absence of breath sounds, but no râles, in the posterior part of the chest below the angle of the scapula on the right side. A diagnosis of infection of the upper respiratory tract, as well as of atelectasis, was made, and roentgen examination of the chest was requested.

The report of the roentgen examination (fig. 1) was as follows: Roentgenographic examination of the chest disclosed a mottled shadow occupying the entire right pulmonary field, which consisted of numerous small, oval areas of decreased density, resembling pockets of air in loops of the intestine and suggest-

Fig. 1.—Roentgenogram showing loops of intestine in the right side of the chest.

Fig. 2.—Roentgenogram showing the stomach and duodenum in a normal position, the loops of intestine in the right side of the chest and the heart and mediastinum displaced to the left.

ing diaphragmatic hernia. Examination of the intestinal tract, with the aforementioned diagnosis in mind, was advised. The right lung and the right leaf of the diaphragm were not visualized. The heart was displaced to the left, which may have been due to the oblique position of the patient. A small portion of the left lung was visualized and appeared to be normal in structure.

The child was admitted to the hospital for further observation.

Physical examination on admission showed that the heart was in a normal position. The findings in the lungs differed from those obtained in the clinic in that diminished breath sounds were heard in the dull area in the right side of the

Fig. 3.—Roentgenogram showing loops of intestine containing barium in the right side of the chest.

chest. In addition, hyperresonance and exaggerated breath sounds were heard over the left lung posteriorly. The next day râles were audible over the involved area in the right side of the chest.

Further roentgenologic studies were made which confirmed the first roentgenographic diagnosis of diaphragmatic hernia. The report of these studies was as follows: Roentgenographic examination of the gastro-intestinal tract disclosed that in the picture (fig. 2) taken immediately after ingestion of the opaque meal the stomach and the first portion of the duodenum were seen in a normal position. The shadow in the right pulmonary field was clearer and suggestive of loops of intestine containing air. A large loop of intestine suggestive of the colon was seen

crossing the region of the outer half of the right side of the diaphragm which was not visualized. The heart was displaced to the left.

Three hours after feeding (fig. 3) there was a large gastric residue. The remainder of the opaque meal was seen in loops of the intestine which were present in the right side of the chest, some of which crossed the middle line and displaced the heart to the left. Six hours after feeding (fig. 4) the loops of intestine were still visualized in the entire right side of the chest. In addition a long loop was seen extending along the right side of the abdomen and entering the right side of the chest in the region of the outer part of the right half of the diaphragm.

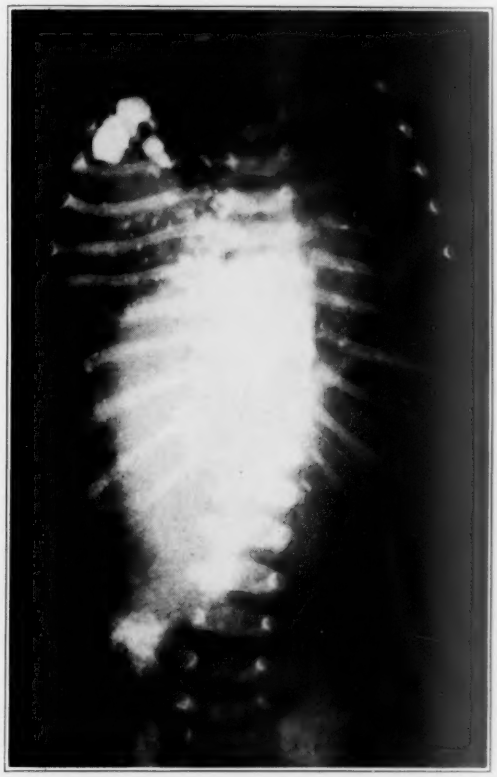

Fig. 4.—Roentgenogram showing loops of intestine containing barium in the right side of the chest.

Fluoroscopic and roentgenographic examinations of the colon with the aid of an opaque enema (fig. 5) disclosed that the sigmoid and the descending colon were present in the right side of the abdomen. The colon then extended into the right side of the chest in the region of the outer half of the right side of the diaphragm. We were unable to fill the entire colon, as the infant began to expel the enema before this could be done.

Roentgenographic Diagnosis.—The roentgenographic findings were those of diaphragmatic hernia. The defect appeared to be in the outer half of the right side of the diaphragm.

Later examinations of the chest on various occasions showed tympany, dulness or even slight resonance. At no time on physical examination was the heart found to be definitely displaced to the left.

Further Course.—The child was given eight feedings daily of 2½ ounces (73.9 cc.) of a mixture consisting of 1 part of water and 2 parts of milk with a 5 per cent solution of cane sugar. He vomited repeatedly during the first twenty-four hours in the hospital, but the next day he retained the feedings. After this he vomited at least once almost every day. The weight increased to 5 pounds and 12 ounces (2,608.2 Gm.), at which level it fluctuated. Because of an apparent loss

Fig. 5.—Roentgenogram taken after a barium enema, showing a portion of the colon in the right side of the chest. The colon passes through the diaphragm in its outer half.

of appetite and increased frequency of vomiting, a more concentrated formula was given in smaller amounts at more frequent intervals, but the vomiting persisted.

The consultant from the surgical service, who saw the child on June 1 at the completion of the roentgenographic studies, advised an attempt to improve the general condition further before performing an operation.

However, improvement did not follow these efforts. Vomiting became more frequent, and the upright position had no effect on it. On June 14 the child began to cough slightly and cried as though in pain. The crying continued on the next

day. A continuous infusion was started because of the loss of fluid. The child became cyanotic; respirations became more rapid, and two days later, on June 17, he died.

Autopsy (Dr. W. Aronson).—Chest: The external appearance of the chest was symmetrical, and no deformities were present. The pleural cavity was approached through a horizontal incision in the eighth right interspace, laterally. On incision of the pleura the cavity was seen to be occupied by intestine. The site at which the intestine passed through the diaphragm was determined by a combined abdominal and thoracic approach. The hiatus consisted of a defect in the diaphragm, located posterolaterally, which was wedge-shaped. It consisted of a sector of a circle, the subtending angle being about 45 degrees. The aortic and the esophageal hiatus were intact. Besides the intestine, the kidney was also partially present in the thoracic cavity. The intestinal herniation involved the entire length of intestine except a portion of the jejunum and sigmoid colon. The left leaf of the diaphragm was normal.

Lungs: The right lung was completely atelectatic and was displaced upward and mesially against the mediastinum. The left lung was displaced posteriorly and laterally and was slightly emphysematous. The anterior portion of the mediastinal septum was thin and deviated to the left. The heart was also displaced to the left. Thus the herniation involved not only the entire right pleural space but a good deal of the left pleural cavity.

Heart: Except for the change in position, the heart showed no abnormalities. The foramen ovale was widely patent.

Abdomen: The liver was seen to occupy a medial position and was also displaced downward. It was moderately enlarged and markedly congested; no other changes were noted.

The stomach was greatly distended; it was situated in the abdomen, with the lower margin reaching the pelvis. The intestine showed no intrinsic changes, and no destruction was apparent.

The right kidney lay partly in the thoracic cavity and partly in the abdomen. The morphologic structure of both kidneys was normal.

Anatomic Diagnosis.—The diagnosis was absence of a portion of the right leaf of the diaphragm; hernia of the abdominal viscera into the thoracic cavity; total atelectasis of the right lung, and emphysema of the left lung.

COMMENT

It is important to note the relative lack of symptoms and typical physical findings in this case, in spite of the amount of the intestine present in the thoracic cavity. The heart did not seem to be pushed to the left, though roentgen examination and later necropsy showed some displacement. In spite of statements that they are almost invariably present, cyanosis, cough and dyspnea were not part of the clinical picture until almost the very end. The appearance of cyanosis and hyperpnea before death probably indicated an increase in the amount of the intestine in the thoracic cavity. Although cough had been present for a short while before admission to the hospital, this was probably due to an infection of the upper respiratory tract.

The hernia in this case falls into the group of those which pass through the foramen of Bochdalek. The condition was due to a failure

of closure of the medial and dorsal portions of the diaphragmatic components. The absence of a sac places it among the false hernias and consequently indicates that there was never complete fusion of the diaphragmatic components, the hernia appearing before the sixth week of embryonic life.

Location of the Kidney.—The location of the right kidney partly above the level of the diaphragm resembles the condition present in a case reported by Kleine and cited by Sanders,[8] in which the left kidney was firmly embedded in a position partially above the diaphragm. The author believed that there had been an exaggerated ascent of the kidney which prevented the closure of the pleuroperitoneal aperture. Later this opening may have become enlarged and have permitted the entrance of the other organs. This explanation does not fit the condition in our case, as the kidney was not firmly fixed to its bed, suggesting a migration secondary to the abnormal diaphragmatic aperture. The large, wedge-shaped opening in the diaphragm was also too extensive to be explained on the basis that the kidney prevented closure of the pleuroperitoneal aperture. It seems, rather, that the dorsal and lateral portions of the diaphragmatic components failed to fuse throughout their whole length.

Enlarged Liver.—As stated in the report of the autopsy in our case, the liver was enlarged. This observation has been made in several other cases of diaphragmatic hernia, but without comment. As the occurrence of hernia on the left side was not investigated in connection with this paper, the reports of only a fraction of the cases described in the literature were read. Yet in spite of the limited number, six other instances were found of congenital hernia with enlarged liver. In one case [3] the peritoneal cavity appeared at autopsy to be almost entirely occupied by a large liver and a distended stomach. Another author [9] reported the cases of two patients with diaphragmatic hernia on the left side, who died in one hour and forty minutes and two days, respectively, after birth. In the first patient the liver extended to the right iliac fossa and into the pelvis, filling almost the entire abdominal cavity. The author stated that the liver of the other patient was markedly enlarged. A case of a 17 year old girl [10] was reported whose liver extended to the brim of the pelvis. An infant who died fifteen weeks after birth [11] showed at autopsy a liver which occupied the whole of the anterior portion of the abdomen. Another infant,[12] who died shortly

8. Sanders, R. L.: Ann. Surg. **91**:367 (March) 1930.

9. Epstein, H. J.: M. J. & Rec. **132**:76 (July 16) 1930.

10. Schisler, E. J.: J. Missouri M. A. **26**:228 (May) 1929.

11. Dodds, G. H., and Flew, J. D. S.: J. Obst. & Gynaec. Brit. Emp. **35**:737, 1928.

12. Waldron, D. H.: Brit. M. J. **2**:1225 (Dec. 31) 1927.

after birth, had an enlarged liver which occupied the whole abdominal cavity.

There seem to be three possible explanations for the enlarged liver seen in conjunction with diaphragmatic hernia in these cases—the enlargement is a coincidence, a result or a cause. Coincidence can be disregarded because of the relatively high percentage of cases in which this association occurred. The increased size of the liver may be a consequence of lowered intra-abdominal pressure and greater available intra-abdominal space, which tends to remove one of the normal restraints to growth. The large liver, however, may well be an etiologic factor in the development of diaphragmatic hernia by raising the intra-abdominal pressure sufficiently to prevent closure of the diaphragm at one of the points of embryonic fusion or to break through the diaphragm at one of these or other points. We are inclined to adopt the last explanation, as we believe that, were enlargement of the liver subsequent to formation of hernia, there would be similar hypertrophy of other viscera, such as the kidney or spleen. In none of the cases cited, moreover, did the hernia pass through a normal diaphragmatic opening. This seems to suggest that some factor operating early in embryonic life, such as increased intra-abdominal pressure, either produced an opening or prevented fusion. The type of diaphragmatic hernia which appears to be the least likely to require increased abdominal pressure for its formation, i. e., that through a normal hiatus, did not occur in any of these cases.

TREATMENT

As far as treatment is concerned, the problem resolves itself into a question of surgical intervention. There is no doubt that life is endangered and that development may be impaired by a herniation of intestine through the diaphragm. Complete obstruction and strangulation are always to be feared. Yet normal development has occurred in the presence of such a hernia.

Since the discovery of diaphragmatic hernia usually is the result of investigation into the cause of the symptoms, surgical intervention will be decided on in most cases, and the problem, therefore, is when to operate. In our case we waited for improvement in the general condition, but improvement did not take place. The decision must be made on the merits of the individual case. Age is not a factor, as successful surgical repair has been made in an infant 41½ hours old [13] and in another infant 7 weeks of age.[14] There are no reported cases of diaphragmatic hernia on the right side in which surgical treatment has been performed, but the reason for this is probably the rarity of the condition.

13. Johnson, H., and Bower, A. G.: California & West. Med. **36**:48 (Jan.) 1932.

14. Robb, E. F.: Journal-Lancet **51**:597 (Oct. 1) 1931.

CONGENITAL ABSENCE OF THE COLON

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On Jan. 21, 1935, a tripara, 30 years old, was delivered without difficulty of an apparently well developed girl, weighing 6½ pounds (2,948.34 Gm.). Six hours after delivery the child vomited a thick, dark greenish, meconium-like material. From this time until death, which occurred three days later, similar vomiting occurred at intervals of from four to eight hours. Water which was given was promptly regurgitated. Forty hours after the birth of the child, the nurse called my attention to the fact that no feces had been passed, although urine was passed in good quantity. Examination of the rectum made at this time digitally and with a catheter revealed a complete closure of the bowel 1 cm. above the anus. The abdomen was markedly distended and tympanitic. Sounds of peristalsis were audible. The pulse rate had increased from 130, at birth, to 160. During this examination approximately one teaspoon of the meconium-like material was vomited.

The child was sent to the York Hospital on January 23. An ileostomy was performed the following day. Death occurred seven hours after the operation.

Autopsy revealed an absence of the entire colon. In place of the colon and proceeding from the cecum was a glistening white cord consisting mostly of fibrous tissue, averaging 4 mm. in diameter and following the course usually occupied by the large bowel. This cord was 28 cm. long and was patulous only for a few millimeters at intervals along its length. The texture of the walls in places suggested that of colonic tissue. The small intestines were grayish green and markedly distended with gas. There were no other malformations.

COMMENT

Congenital malformations of the intestines are not frequent. However, when malformations do appear, the rectum and anus are the most favored sites. Any portion of the intestines may present atresia, but the condition occurs most frequently in the duodenum. Anomalies appear less frequently in the colon than in any other part of the intestines. A search of the literature revealed no report of a case, such as I have described, in which there was complete congenital absence of the colon.

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Progress in Pediatrics

THE CHILD'S HEART IN AVITAMINOSIS

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Recently while attending a pathologicoclinical conference devoted exclusively to the demonstration of material obtained from children at autopsy, which is conducted once each month by Dr. Richard H. Jaffé, director of the department of pathology of the Cook County Hospital in Chicago, I was much impressed by the gross demonstration of several infants' hearts. The first specimen, from a baby 4 months old, showed marked hypertrophy and dilatation. The musculature was reddish brown and occupied a large space in the thoracic cavity. Before death the child presented symptoms of cyanosis and marked dyspnea. Dr. Jaffé thought that the condition shown by this specimen belonged to the yet unexplained group of idiopathic cardiac hypertrophies.

The second specimen came from an infant about 7 months old who had suffered from a severe anemia. The heart was pale, whitish and markedly increased in size. The right heart was dilated, though the myocardium was not as firm as in the former case. Careful postmortem examination, including the inspection of bone marrow and of the spleen, as well as of lymphatic tissues, threw no light on the nature of the anemia. Examination of the blood during life gave results corresponding to the findings in a severe case of secondary anemia.

I became reflective about the possible nature of these unexplained morbid processes. I recalled that formerly as a member of the attending staff in hospital service I was not infrequently approached by a younger member of the house staff and asked to suggest a subject for investigation or for a paper. Unless I had something definitely in mind, I often told the young man to note carefully on his daily rounds among his patients all the facts about a certain disease which were known or thought to be known and, on the contrary, all points which were in doubt or unknown. Then I suggested to him that if he would take for his subject one of the unknown facts about a certain disease and work with the idea of solving the problem, he not only would become a discoverer but would also learn the technic and methods of original investigation. It is needless to say that only a few of the young men were eager to adopt my suggestion.

Read at Beth Israel Hospital, New York, Feb. 27, 1935.

Nevertheless, I left Dr. Jaffé's clinical conference stimulated by his interesting and lucid demonstration with the determination that I would review the literature with the hope of ascertaining what was already known about the effect of avitaminosis on the infant's heart and also what points were still unknown. While I was making this review, I was honored by an invitation to speak before the members of the staff and the alumni of Beth Israel Hospital, and I decided to present certain aspects of the topic this evening.

THE HEART IN BERIBERI

Certain changes in the heart occur in various types of vitamin deficiency. These changes are probably most striking in B avitaminosis, well illustrated by the beriberi of nurslings. It has been suggested that there is a similarity between the heart of the spasmophilic nursling with manifest tetany and that of the infant with B avitaminosis. Reyher [1] thought this to be the case because in both conditions there is enlargement of the right heart. He stressed this point by citing a case reported by Thiemich of an infant, 6½ months old, with manifest tetany who showed marked dilatation of the heart, pulmonary edema and advanced passive congestion in various organs. Reyher reported two autopsies of his own which showed degenerative atrophic changes in nerves and muscles such as are observed in beriberi. In both cases there were severe dilatation and hypertrophy of the heart. In the first case the right heart was most severely involved. He concluded, therefore, that there is a certain relationship between spasmophilia and beriberi. He found that if vitamin B, especially the antineuritic factor, is administered to patients with this condition a definite improvement results.

Schiff,[2] who verified the occurrence of cardiac enlargement in a parathyroidectomized dog with tetany, considered the dilatation to be due to irritation of the vagus and not muscular in origin.

Some authors have noted that a relationship may exist between celiac disease and beriberi. Haas [3] observed that beriberi may occur in infants who have suffered from celiac disease. He expressed the opinion that the symptoms of beriberi are secondary and due to anorexia, the form of diet and a deficiency of vitamin B. Lehndorff and Mautner,[4] in discussing celiac disease, also considered the question of avitaminosis in association with cardiac hypertrophy and dilatation. They stated

1. Reyher, P.: Zum Spasmophilieproblem, Klin. Wchnschr. **2**:163 (Jan. 22) 1923.

2. Schiff, E.: Das Spasmophilie Herz, Acta pædiat. **3**:57, 1923.

3. Haas, S. V.: Beriberi in Late Infancy; the Result of Celiac Disease, Arch. Pediat. **46**:467 (Aug.) 1929.

4. Lehndorff and Mautner: Die Coeliakie, Ergebn. d. inn. Med. u. Kinderh. **31**:456, 1927.

the belief that not only vitamin B but also vitamin C may be lacking in children suffering from celiac disease, because of the resulting symptoms of inadequate nutrition. Consequently a lesion of the heart similar to that which occurs in beriberi or scurvy may occur as a secondary manifestation in celiac disease.

Wenckebach,[5] who has studied beriberi, particularly the condition of the heart, for many years, has written principally on the adult type of cardiac involvement in this disease. Like all other investigators on the subject, he is convinced that the cause of the disease is an absence of vitamin B from the diet and that it occurs largely in areas where polished rice is the exclusive food of the people. The disease is common among persons of every age in the Orient, and in infancy it stands in close relation to the nutrition. The history of the mother during pregnancy, particularly during the last month, is of enormous importance, for she may present symptoms of vitamin B deficiency, such as palpitation and creeping sensations in the inferior extremities. She may also show weakness of the legs and slight edema of the ankles, indicating mild beriberi.

When the disease occurs in breast fed infants, as it frequently does in affected districts, it is probable that the baby acquires the disorder because the milk of the mother is very deficient in vitamin B. It is well known that the diet of many oriental mothers consists of rice, some meat or dried fish and very few vegetables. Such a diet is deficient not only in vitamin B but in vitamin A and D as well.

Vedder [6] noted that polished rice is not the only food which may produce beriberi. He stated that it has been shown that a number of other foodstuffs are either relatively or absolutely deficient in the vitamin which prevents beriberi. Highly refined white wheat flour and various foods rich in carbohydrates, such as tapioca, sago and various sugars, are quite as deficient as rice, and consequently when used exclusively in the diet will produce beriberi with great certainty. Vedder also noted that sterilized and canned foods may be deficient in vitamin B, though he emphasized the fact that whole rice, whole wheat, beans and barley, if used in sufficient amounts, will prevent the disease.

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5. Wenckebach, K. F.: Herz- und Kreislaufinsuffizenz, in Grote, L. R.; Fromme, A., and Warnekros, K.: Medizinische Praxis, Dresden, Theodor Steinkopff, 1932, vol. 12; St. Cyres Lecture on Heart and Circulation in Tropical Avitaminosis (Beri-Beri), Lancet **2**:265 (Aug. 11) 1928; The Riddle of the Beriberi Heart, in Contributions to the Medical Sciences in Honor of Dr. Emanuel Libman by His Pupils, Friends and Colleagues, New York, International Press, 1932, vol. 3, p. 1199.

6. Vedder, E. B.: Beriberi, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1923, vol. 2, p. 815; The Deficiency Diseases and the Vitamins, Porto Rico J. Pub. Health & Trop. Med. **5**:458 (June) 1930

Ohta,[7] writing on beriberi at the Charity Hospital at Tokyo, admitted that the infantile type occurs largely among breast-fed infants, though he found that it may occur in artificially fed children. In the University Children's Clinic at Tokyo there were 16 young children with this condition among 430 who were artificially fed. Ohta and others observed that a group of children who were fed mainly starches tended to fall ill with the disease. Ohta also observed that beriberi occurred with greatest frequency in infants from 2 to 3 months old. It was noted in children from the fourth to the eighth month, though the number of cases was less than in the first period mentioned. He called attention to the fact that the diagnosis of the condition in infants less than 1 month old is difficult because in this period the symptoms are incomplete, though he remarked that he recently diagnosed a condition as beriberi in an infant 9 days old. It is a matter of general observation in the Orient that the disease occurs most frequently in the hot season of the year, particularly during July and August, though Ohta stated that at the clinic in Tokyo some patients are admitted in winter.

Wenckebach summarized the pathologic findings for the adult type of berberi as follows: 1. Degenerative processes take place in the peripheral nervous system, damaging or destroying the peripheral motor and the sensory tract, as well as the sympathetic and the parasympathetic nerve tracts. The symptoms are those of extensive polyneuritis. 2. Anasarca and serous effusions occur in the large cavities of the body. In chronic cases there may be a condition of extreme general atrophy and dryness of skin or tissues, the so-called dry form. 3. Heart disease characterized by general feebleness of the circulation, palpitation on the slightest exertion and swelling of the liver, with edema of the extremities, is present. Heart failure is often the cause of death.

Wenckebach stated that at the beginning of the disease the whole heart, the right side as well as the left, is enlarged. A roentgenogram shows that the left ventricle is clearly larger than normal. It is not possible to decide at this stage whether the enlargement is due to dilatation alone or to hypertrophy of the wall of the muscle. The enlargement and consequent failure of the heart may occur suddenly or gradually. In the later stage the right heart is principally involved. The existence of hypertrophy and dilatation of the right heart has been verified on both clinical and postmortem examination by all who have studied the disease. Wenckebach also pointed out that with increasing weakness of the heart stasis occurs in the liver and the venae cavae, the liver becomes swollen, and ascites and, not infrequently, sudden death occur. He called attention to the fact that there is no irregularity of the

7. Ohta, K.: Zur Klinik der Säuglingsberiberi, Jahrb. f. Kinderh. **128**:1 (June) 1930.

heart, no extrasystoles, flutter or fibrillation. The electrocardiogram may show a certain degree of right ventricular preponderance, though no other significant findings are observed.

It is stated by most investigators that the anatomic changes in infantile beriberi do not differ materially from those in the adult type. The right heart is greatly hypertrophied and dilated and forms much the larger part of the child's heart.

Vedder observed that the wall of the right ventricle in this disease may measure from 5 to 7 mm. in thickness, while the wall of the left ventricle measures only from 3 to 5 mm. General anasarca is not uncommon. A clear fluid, sometimes of a greenish tint, is found in the pericardial cavity. Degenerative changes in nerve fibers are less marked than in the adult type of beriberi.

The infantile type, according to José Albert[8] of Manila, affects largely breast-fed infants and is a cause of high infant mortality in the Philippine Islands. He recognized three types: (1) the aphonic; (2) the pseudomeningeal; (3) the cardiac. The cardiac type gives rise to the severest symptoms.

Ohta, commenting on the classification of beriberi in infants, observed that various symptoms may predominate, such as edema and paralysis; there may be cerebral and mixed forms, but he remarked that the clinical types are variable and there may be a transition from one type to another from day to day.

Wenckebach, discussing the varieties of heart involvement in beriberi, recognized a chronic, and an acute or so-called pernicious and usually fatal, form. The latter type is now much less frequently seen than formerly, since specific treatment has diminished it.

The multiplicity of cardiovascular symptoms is characteristic of infantile beriberi. The first sign of circulatory insufficiency is the instability of the pulse rate, which becomes more rapid if the child cries or is otherwise active. The respiratory rate fluctuates with the pulse rate. Early in the disease there is increasing pallor and breathing is somewhat difficult. Shortly thereafter a definite dyspnea may be observed. The second pulmonic tone becomes markedly accentuated. It may be heard over the sternum, denoting dilatation of the right heart and increased pressure of the pulmonary circulation, although the systemic blood pressure is very low. The dilatation may be verified by roentgen examination. In the severer cases it may extend considerably beyond the right sternal border and is readily demonstrated by percussion. In the grave cases the heart tones have a gallop rhythm. With development of the changes in the cardiac muscle the dyspnea becomes

8. Albert, José: Cardiac Beriberi in the Nursling, Monatschr. f. Kinderh. **54**:80, 1932.

more marked, the accessory muscles of respiration come into action, the ala nasi spread rapidly, and respiratory retraction of the thorax is observed. If the child cries during this stage of the disease, pallor increases, cyanosis is noted, and the child grunts with each respiration. The so-called Shoshin attacks may occur, and they indicate the acute stage of the disease, characterized by unpleasant palpitations of the heart on slight movement or on psychic disturbance or perhaps even in a state of rest; the Shoshin condition indicates severest involvement of the circulation. During such an attack the child becomes extremely pale, and the voice is feeble and whispering. Frequently the infant contorts his face and moans pitifully, as though in greatest pain. He becomes apathetic and very soon comatose; the extremities become cold, and the infant is bathed in perspiration. Sometimes there are twitchings of the extremities, and the head is retracted; occasionally high fever may occur. Dyspnea becomes more and more severe, and death ensues. Sometimes before death tones are heard over the femoral and brachial arteries and over other large vessels.

In Dr. Jaffé's clinical conference the subject of the condition of the heart in beriberi was briefly referred to, and the opinion of one of the younger physicians was that beriberi could not be thought of in the case in question because there were no symptoms of neuritis. In infants, however, only the objective symptoms can be recognized, though the intense suffering of these patients may suggest the presence of neuritis. Much of the distress is undoubtedly caused by cardiac dilatation with its accompanying respiratory embarrassment.

In this connection I wish to report, for the purpose of comparison, the case of a girl who lived to be 8 months of age.

The child was born under favorable circumstances and came from well-to-do, healthy, young parents. A sister aged about 6 had died several years before of a pneumococcic peritonitis. The mother was well during the last pregnancy, though she restricted her diet considerably. The baby seemed normal at birth, had been artificially fed from the first and had gained moderately in weight. When she was 3 months old, it was found that she was extremely difficult to feed. At times her struggles against feeding were so severe that she became prostrated and moderately cyanotic. In the interim she was happy and slept normally, though she showed a slight pallor and failed to make satisfactory gain in weight. The baby was repeatedly examined. When she was 6 or 7 months old, there seemed to be a slight increase in the cardiac area, the increase being most marked toward the right. One morning, when she was 8 months old, she became suddenly ill with marked dyspnea, coughing, cyanosis, groaning and crying as though in agonizing pain. The temperature was moderately elevated. The pulse rate was weak and exceedingly rapid. Physical examination showed a definite increase in the cardiac area, a soft systolic murmur at the apex and numerous small fine râles over the posterior portion of the left lung. The dyspnea became extreme. The cyanosis increased, and the baby's suffering, as evidenced by her groans and cries, was almost indescribable. In this condition she died. I performed the autopsy at

the home of the patient shortly after death. On opening the thorax I was amazed at the size of the heart. The measurements, which were afterward confirmed, were 8.5 by 5.5 by 5.5 cm. I brought the thoracic viscera to the laboratory of the Michael Reese Hospital, where the specimen was examined and described by Dr. Oscar T. Schultz, who was at that time the pathologist. He found that the coronary arteries were markedly curled and prominent and felt firm. The heart was generally enlarged and felt soft. The left ventricle, as well as the right, was markdely distended. On the cut surface the cardiac muscle appeared yellow and in other areas was reddish brown. The musculature was not colored uniformly. The papillary muscles were flat and soft; the right auricle was nearly empty and the foramen ovale closed. The apex of the heart was increased in size as though formed by both ventricles. The microscopic examination of the heart showed that the muscle fibers were separated as though they had been pulled apart. The normal markings of the fibers were indistinct. The endocardium in some places was edematous and separated from the muscle. There was a general congestion of the myocardium.

As I have already noted, this case is presented only for comparison. The diagnosis of idiopathic cardiac hypertrophy was accepted as the correct one, though no adequate explanation of this condition is at hand. Status lymphaticus, thymic enlargement, or involvement of the endocrine system offers no satisfactory explanation. In the excellent review by Kugel and Stoloff [9] it is pointed out that idiopathic hypertrophy may be due to a number of causes, such as renal disease, congenital heart disease, anomalous origin of blood vessels, any infectious disease which may produce myocarditis, hypertension in the mother during pregnancy, as shown by the clinical history, and myocardial changes of inflammatory nature. To refer again to the pathologic changes of the heart in beriberi, Wenckebach mentioned those occurring as a result of toxic degeneration. Microscopic examination of the myocardium shows hyaline and fatty changes in the muscle or fibrosis. There may be fragmentation of the muscle fibers. If one compares these histologic changes with those described for idiopathic hypertrophy by Kugel and Stoloff, one recognizes a striking similarity. The same changes of the muscle fibers, with fatty infiltration, muscle degeneration and replacement fibrosis are observed. It would appear that the histologic changes in beriberi differ only slightly from those described for idiopathic cardiac hypertrophy. The history in most of these cases shows that the disease is not congenital but occurs after birth following a short period of apparent well-being.

If one compares the clinical history of this child suffering from idiopathic cardiac hypertrophy with that of a patient suffering from the cardiac condition in beriberi, one notes a striking clinical similarity. It is true that postmortem examination shows that in beriberi the right

9. Kugel, M. A., and Stoloff, E. G.: Dilatation and Hypertrophy of the Heart in Infants and in Young Children, Am. J. Dis. Child. **45**:828 (April) 1933.

ventricle of the heart is most severely involved, while in idiopathic hypertrophy both sides of the heart are attacked, the hypertrophy and dilatation of the left ventricle sometimes predominating. In every case of idiopathic cardiac hypertrophy in a child, the health of the mother during pregnancy and particularly her diet should be inquired into to determine whether she received an adequate supply of vitamins in her food. It should also be determined, if possible, whether there was a deficiency of vitamin B in the baby's diet.

In the patient whom I have just described, the conditions necessary for causing a vitamin B deficiency were at hand. The mother restricted her diet to a considerable extent during pregnancy. On account of the severe anorexia from which the baby suffered inanition occurred, and the baby's intake of vitamin B, as well as that of other vitamins, was necessarily diminished. Anorexia and inanition are commonly observed in infantile beriberi.

In a review of the literature on the antineuritic vitamin by Kruse and McCollum,[10] it is pointed out that all concentrates and even crystals of the antineuritic vitamin thus far reported have been shown to be contaminated by the presence of other components of the B complex. Nevertheless, potent B fractions have been separated. Thus Seidell [11] obtained an active product which was capable of relieving polyneuritis in rats. In 1926, Jansen and Donath [12] isolated a crystalline material which protected rice-birds against polyneuritis; later Williams [13] and his co-workers tested crystals of vitamin hydrochloride furnished by Jansen and Donath from pigeons which had been fed a diet of polished rice. The crystals prevented the appearance of polyneuritis. Wenckebach is inclined to think that the highly purified vitamin B preparation of Jansen and Donath acts as a cardiac hormone or automatin counteracting the injurious effect of vitamin B deficiency on the heart. Perhaps some day when the specific vitamin B substance is more available for use its presence or absence in the fluids and organs of the body may be determined quantitatively and the degree of vitamin B deficiency ascertained accurately.

I realize that by offering a comparison between the condition of the heart in beriberi and idiopathic hypertrophy I am treading on thin ice.

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10. Kruse, H. D., and McCollum, E. V.: Review of Recent Studies on the Antineuritic Vitamin, J. A. M. A. **98**:2201 (June 18) 1932.

11. Seidell, A.: Further Progress Towards Isolation of Antineuritic Vitamin (Vitamin B) from Brewers' Yeast, J. Biol. Chem. **82**:633 (June) 1929.

12. Jansen, B. C. P., and Donath, W. F.: K. Akad. v. Wetensch. Amsterdam versl. **35**:923, 1926.

13. Williams, R. R.; Waterman, R. E., and Gurin, Samuel: Jansen and Donath Procedure for Isolation of Antineuritic Vitamin, J. Biol. Chem. **87**:559 (July) 1930.

though it is not beyond the range of possibility that the sporadic occurrence of idiopathic cardiac hypertrophy may be due to vitamin B deficiency. In the absence of anatomic, infectious and other organic causes, I take the liberty to suggest this possibility as a tentative hypothesis.

THE HEART IN INFANTILE SCURVY

At Dr. Jaffé's clinicopathologic conference the clinical history recorded the fact that the second child had suffered from a severe secondary anemia, the exact nature of which was not determined.

As a rule the hemoglobin is greatly diminished in infantile scurvy, though Alfred Hess [14] referred to a group of cases of this disease characterized by polycythemia, which may persist after other signs of the disorder have disappeared. It has been pointed out that the red cells may rise to over six or seven million per cubic millimeter and the hemoglobin to 110 or 120 per cent. The anemia of infantile scurvy is usually chlorotic, though nucleated red cells are occasionally present. The platelets are increased in some instances, especially in those in which polycethemia occurs. In these cases the increase in the number of platelets seems to parallel the increase in the number of red cells. Most observers of infantile scurvy have noticed the extreme pallor which may precede the typical clinical manifestations. Since the anemia may occur during the prescorbutic stage, the older view which regarded it as due to loss of blood is no longer tenable.

Aron [15] stated the belief that the anemia of scurvy is characterized by a reduction of the hemoglobin content as well as of the red cells, and he expressed the opinion that an alimentary injury, possibly due to lack of vitamin C, inhibits the hematopoietic function of the bone marrow and produces the anemia. Recent investigations indicate that the absence of vitamin C itself does not produce the anemia, though Aron pointed out that with the cure of the scurvy the anemia rapidly improves.

The earlier observers did not note any cardiac changes in scurvy, though Darling [16] described enlargement of the right heart in this disease. Hess,[14b] several years ago, observed that enlargement of the heart, more especially of the right ventricle, was a frequent occurrence. He elicited this enlargement at the bedside and verified the finding in

14. (*a*) Hess, A. F.: Rickets, Including Osteomalacia and Tetany, Philadelphia, Lea & Febiger, 1929, p. 234; (*b*) Scurvy, Past and Present, Philadelphia, J. B. Lippincott Company, 1920; (*c*) Recent Advances in Knowledge of Scurvy and the Antiscorbutic Vitamin, J. A. M. A. **98**:1429 (April 23) 1932.

15. Aron, Hans: Die Nährschäden des Kindes, ihre Entstehung, Verhütung und Heilung, Berlin, Urban & Schwarzenberg, 1928.

16. Darling, S. T.: The Pathologic Affinities of Beriberi and Scurvy, J. A. M. A. **63**:1290 (Oct. 10) 1914.

numerous cases by roentgen examination. He noted at the same time a marked broadening at the base of the heart at the site of the large blood vessels. In this way the cardiac enlargement in scurvy resembled somewhat that which occurred in beriberi.

Hess quoted Schoedel and Nauwerk,[17] who reported five autopsies with the following observations: An increased amount of pericardial fluid was sometimes observed; both ventricles were moderately dilated, and the right ventricle was somewhat hypertrophic. In other cases the right ventricle was dilated and slightly hypertrophied and the muscles were pale and tough. The heart action was rapid and the respiration proportionately increased. The heart rate was increased by slight exertion or excitement. Salle and Rosenberg[18] reported the occurrence of hemorrhagic pericardial effusion in patients confined in a Russian dungeon. Three hundred such cases were observed during six months.

Erdheim[19] of the Pathological Institute of Vienna had an unusual opportunity to dissect many patients who died of scurvy during the post-war period. Aside from the skeletal changes which he described, he directed special attention to the changes in the heart, which consisted for the most part of hypertrophy of the right ventricle. He reported that hypertrophy was present in two thirds of the patients whom he examined. In the remaining cases no enlargement was noted, though in some of the records the cardiac findings were not mentioned. In those cases in which no enlargement was noted, the disease was in the incipient phase or of a mild variety. Erdheim concluded as a result of his investigation that cardiac hypertrophy should be considered a typical occurrence in the course of infantile scurvy. In this condition the right heart was always hypertrophied, though not always dilated. In the severer cases the walls of both ventricles were hypertrophied. The degree of hypertrophy varied with the severity of the scurvy, though in some instances there was only a moderate hypertrophy in a mild case and in other instances, considerable hypertrophy in a mild case. Erdheim also observed that exceptionally in young infants only a moderate hypertrophy was observed, whereas in older children the enlargement was nearly always present. In those infants who were markedly emaciated, with pronounced marasmus, extreme cardiac hypertrophy was usually noted.

In those cases in which insufficiency of the heart developed, the liver almost invariably showed evidence of stasis. Hepatic stasis, how-

17. Schoedel, J., and Nauwerk, C.: Untersuchungen über die Möller-Barlowsche Krankheit, Jena, Gustav Fischer, 1900.

18. Salle, V., and Rosenberg, M.: Ueber Skorbut, Ergebn. d. inn. Med. u. Kinderh. **19**:86, 1921.

19. Erdheim, J.: Ueber das Barlow-Herz, Wien. klin. Wchnschr. **31**:1293, 1918.

ever, was also observed in cases of infantile scurvy in which no cardiac hypertrophy was demonstrated.

In all of the patients with Barlow's disease whom Erdheim examined, the capacity of the thorax was not diminished by malformation. In no case was there a deformity of the thorax such as is found in rickets which could cause pressure on the vessels or interfere with cardiac movement. Erdheim explained the enlargement of the heart in scurvy by stating that osseous changes occur involving principally the ribs; when these changes have progressed far enough, or when subperiosteal hemorrhages have occurred, thoracic pain results. In this condition, respiration is inhibited because the ribs and intercostal muscles voluntarily restrict their movement. Consequently the thorax does not expand as it should normally, and the pumping of the blood into the pulmonary capillaries is effected exclusively by the muscular effort of the right ventricle. If this view is correct, it is obvious that a compensatory hypertrophy of the right ventricle takes place. Erdheim stated the belief that this theory is possible on the basis of anatomic conditions, though he expressed the opinion that further clinical investigation and physiologic experimentation may throw more light on this subject.

In the light of recently acquired knowledge it should be possible to determine qualitatively or quantitatively the amount of cevitamic acid in the fluids or organs of the body. This substance is also known in the literature as ascorbic acid and is regarded as crystalline vitamin C. If at autopsy one were to examine the cardiac muscle for this substance and find it greatly diminished or absent, one would suspect that the cardiac hypertrophy or dilatation was due directly in some way to the vitamin deficiency in this particular organ.

Various histologic changes of the heart in scurvy have been reported. The early investigators observed fatty degeneration of the cardiac muscle, atrophy of the musculature and subpericardial hemorrhages. Aschoff and Koch [20] observed that in some cases the musculature was well preserved but decidedly pale. In other cases they reported a general atrophy of the cardiac fibers, with a deposit of pigment, and in still other cases, an increase of connective tissue.

Höjer [21] examined the cardiac muscle of nineteen guinea-pigs, thirteen of which had suffered from scurvy. He concluded that the heart shows the same histologic changes as the skeletal muscles, consisting of hyperemia and atrophy. Occasionally necrosis is observed, followed by calcification. He noted that these changes appeared during the latent stage of scurvy. Some investigators have reported that no notable histologic changes are present in the cardiac muscle.

20. Aschoff, L., and Koch, W.: Skorbut, Jena, Gustav Fischer, 1919.

21. Höjer, J. A.: Scurvy, Acta pædiat. (supp.) **3**:8, 1924.

Erdheim made the pointed remark that in the occurrence of hypertrophy or dilatation of the right heart which cannot be explained by other causes, the possibility of the presence of latent Barlow's disease should be considered.

In this connection it is most interesting to refer briefly to the recent experiments on animals conducted by Rinehart and Mettier,[22] and also by Stimson, Hedley and Rose [23] of the United States Public Health Service.

Rinehart and Mettier produced scurvy in guinea-pigs, and when the disease was well established, they inoculated the animals with an organism they designated as the beta-streptococcus. They were able to produce cardiovalvular lesions. They maintained that the endocarditis which they produced experimentally is similar to that which occurs in acute rheumatic fever in man. Furthermore, they claimed that the degenerative and proliferative lesions in the cardiac muscle and pericardium of experimental animals made scorbutic and then infected with streptococci are similar to those described by Aschoff for rheumatism. Other organisms than the beta-streptococcus may produce cardiac lesions if scurvy has previously existed in the experimental animal. These authors maintained that infection alone or scurvy alone will not produce the cardiac lesions which have been referred to. But when scurvy and infection are combined, characteristic lesions will be produced in the valves of the heart. The authors advanced the theory that vitamin C undernutrition may be a necessary factor in the development of rheumatic fever. They reported that a subcutaneous nodule similar to the subcutaneous nodule occurring in rheumatic fever was observed in one experimental animal. They also consider that a scorbutic state may be the basis of hemorrhagic manifestations sometimes observed in rheumatic fever.

Stimson and his associates confirmed the work of Rinehart and Mettier and, before proceeding, constructed a working hypothesis as a guide to their experimental work. They assumed that rheumatic fever is a disease of temperate climates and is more prevalent in the colder sections; that on this continent it occurs during the late winter and early spring, and that it prevails mostly among the poorer classes, especially among those who live at home. Those who are removed from home and placed under good institutional care rarely have rheumatic

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22. Rinehart, J. F., and Mettier, S. R.: The Heart Valves and Muscle in Experimental Scurvy with Superimposed Infection, Am. J. Path. **10**:61 (Jan.) 1934. Rinehart, J. F.; Connor, C. L., and Mettier, S. R.: Further Observations on Pathologic Similarities Between Experimental Scurvy Combined with Infection and Rheumatic Fever, J. Exper. Med. **59**:97 (Jan.) 1934.

23. Stimson, A. M.; Hedley, O. F., and Rose, E.: Notes on Experimental Rheumatic Fever, Pub. Health Rep. **49**:361 (March 16) 1934.

fever. The disease is more common in the cities than in rural districts. The age at which first attacks occur is after the fourth or fifth year. Streptococci play an important, if not an essential, rôle in the etiology. Stimson and his associates produced vitamin A deficiency in a number of animals and then inoculated them with streptococci, with negative results. They then proceeded to produce scurvy in guinea-pigs by diets deficient in vitamin C and inoculated the animals with streptococci. At first they obtained no results. They thought that the organisms which they used lacked specific pathogenicity. Later, however, they obtained an organism which when injected into scorbutic guinea-pigs gave cardiac reactions similar to those described by Rinehart and Mettier.

Stimson and his co-workers found that by injecting streptococcus exotoxin into scorbutic guinea-pigs, without the introduction of the living organisms, endocardial and myocardial lesions could be produced. This point is of interest, and if correct indicates that rheumatic and cardiac lesions may be produced by the toxins of streptococci. The fact that Stimson and his associates could confirm the experiments of Rinehart and Mettier adds significance to the observations in both investigations. One may be pardoned if one reflects how curious it is that in the vast number of cases of scurvy of the infantile and the adult type among human beings many generations of clinicians and pathologists should have overlooked the presence of rheumatic endocarditis such as has been found in guinea-pigs. A scientist, however, must be open-minded and await final results.

To return for a moment to Dr. Jaffé's case, the question of whether the infant with severe anemia and cardiac hypertrophy and dilatation whom he demonstrated suffered from a vitamin C deficiency or latent infantile scurvy is altogether conjectural. For the purpose of discussion, I have assumed in the absence of other findings that the case might have been one of the latter condition.

ENLARGEMENT OF THE HEART IN RICKETS

It has been known for a long time that severe rachitic deformities of the bony thorax, such as those reported by Park and Howland,[24] may constitute a veritable menace to life. In this condition the thorax is not symmetrically deformed but is often markedly asymmetrical. It is observed that the clavicles are prominent and grotesquely bent. The manubrium is prominent and appears to be elevated. The sternum itself is thrust forward and not infrequently sharply curved or bent. The xiphoid process often points directly backward. The costal margins flare outward. The lateral portions of the thorax are depressed; the

24. Park, E. A., and Howland, J.: Dangers to Life of Severe Involvement of the Thorax in Rickets, Bull. Johns Hopkins Hosp. **32**:101 (April) 1921.

costal arch is always higher on one side than on the other, and consequently the flaring is unequal. If in these severe cases of rickets the child sits erect, the spine may be observed to be bent in any direction. There may be at one time lordosis in the upper portion, or kyphosis below, with well marked scoliosis. As a result of these several deformities the thorax becomes divided into two communicating chambers. In the anterior chamber the heart is imprisoned. When the heart is removed, the left ventricle appears to be normal in size, but the right appears dilated and hypertrophied, though in some instances the left ventricle also may be hypertrophied. The heart is disproportionately large for the size of the thorax, often appearing enormous in comparison with the latter.

Park and Howland also observed in rats rendered rachitic by faulty diet that deformities of the thorax occurred similar to those in infants; consequently the heart enlarged, the lungs collapsed and bands of atelectasis were noted. Severe rickets in infants is less frequently encountered now than in former years, especially in those regions where prophylaxis is generally practiced, though in rachitic children who suffer from protracted bronchopneumonia, adhesive pleurisy or atelectasis, hypertrophy and dilatation of the right heart may occur, even when there are no severe deformities of the bony thorax. It has long been known as a clinical fact that scoliosis with thoracic deformity may produce hypertrophy of the right heart.

It is not this group of cases that I wish to stress, but more particularly the cardiac changes in cases of rickets without severe deformities of the thorax or spine. Sir William Jenner, in his clinical lectures "On Rickets, Tuberculosis, and Abdominal Tumors," in discussing the pathology of the heart in rickets referred to the white patches which he commonly observed on the visceral pericardium of rachitic children. He said that in some instances the spots were opalescent, owing to a thickening of the pericardium, and some appeared as shaggy growths from the surface. Jenner stated the belief that these white patches occur in children whose chests are deformed from rickets and that they occur over the left ventricle a little above the apex, just at the spot which impinges against the fifth rib. He was of the opinion that these white patches are due to the friction of the pericardium against the ribs. He also recognized that the apex of the heart frequently lies outside the nipple line, but he hastened to say that he did not consider this due to hypertrophy of the left ventricle, but to malposition of the heart on account of the changed condition of the thorax.

Pfaundler [25] stated that the smooth muscle as well as the cardiac muscle may undergo a form of myopathy in rickets, just as atony of

25. Pfaundler, M.: Mangelkrankheiten, in Feer, E.: Lehrbuch der Kinderheilkunde, Jena, Gustav Fischer, 1930, p. 193.

the gastro-intestinal muscles and of the abdominal wall produces distention. As careful an observer as Finkelstein [26] recorded that so far as he had noted reports of this condition in the literature [27] little was stated about hypertrophy of the right heart in rickets, though he himself had seen this condition frequently at autopsy. He noted further that in all of the more severe cases in which thoracic rickets and chronic indurative pneumonia were present this cardiac hypertrophy and dilatation occurred. He made the statement that it was frequently possible for him to recognize cardiac enlargement during life, He was able to elicit an increased area of cardiac dulness and a widened and forcible apex beat. A number of these patients died after presenting typical symptoms of cardiac asthma with cyanosis, edema and swelling of the liver and of the spleen. On the other hand, Finkelstein reported the case of a boy 1½ years old who had well defined rickets, and in whom it was possible to demonstrate by roentgenograms considerable enlargement of the heart, a rapid pulse rate and a persistent increase in respiration. This condition lasted for two years, after which the child became normal. Finkelstein made the reservation that further observations of cardiac changes in rickets are necessary. He also expressed the opinion that the remote effects on the heart and circulation which may occur in later life should be investigated before definite conclusions are drawn.

Hess [14a] supported the view expressed by Finkelstein, though he added that a primary hypertrophy of the right heart takes on added interest and significance in view of the fact that this condition has been found both clinically and at necropsy in cases of infantile scurvy and beriberi. He did not recall observing cardiac enlargements in his own examinations of a large series of roentgenograms of rachitic infants.

Perhaps the most frequently quoted investigator in recent years on this subject is Karl Meixner,[28] who wrote on the enlargement of the left ventricle in rickets. He was working in the Medico-Legal Institute of Vienna and collected the hearts of rachitic children over a period of ten years. In addition, he preserved several bones from each child to verify the rachitic changes. In some of the hearts enlargement was not immediately apparent, though on closer observation the globular form of the left ventricle could be recognized. He found a general widening of the left ventricle in all cases, though in varying

26. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, Berlin, H. Kornfeld, 1924, p. 659.

27. Stoeltzner, W.: Pathologie und Therapie der Rachitis, Berlin, S. Karger, 1904, p. 87. Veil, W. H.: Herzmuskel und Herznervenkrankheiten, Neue deutsche Klin. **4**:758, 1929.

28. Meixner, Karl: Enlargement of the Left Ventricle in Rickets, Wien. klin. Wchnschr. **41**:1273 (Sept. 6) 1928.

degree. Richter,[29] writing from the medicolegal standpoint, observed that among 300 children who died suddenly during a year he found 20 or 30 who showed cardiac hypertrophy from various causes, and Kolisko,[30] who was the chief of the Medico-Legal Institute of Vienna, found a considerable number of rachitic children with cardiac hypertrophy. Kolisko took a conservative position and was not willing to admit a causal relationship between rickets and cardiac hypertrophy.

While Meixner acknowledged the possibility of enlargement of the left ventricle in nonrachitic children, nevertheless in the eleven specimens of hearts from rachitic children which he collected and studied carefully there was no other adequate explanation for the enlargement, nor was there evidence of diphtheria or other exanthematous diseases. Seven of the 11 children whom he examined were less than 1 year of age, 3 being only 4 months old. Four were in their third year. Most of his specimens came from children who were markedly underweight.

In a few of his patients in whom there was severe deformity of the thorax there was also enlargement of the right heart, which was undoubtedly due to obstructed respiration. Nevertheless, in one of these patients with deformity of the chest and dilatation of the right heart there was also hypertrophy of the left heart. The thickening of the endocardium was noted nearly always in the cases of ventricular hypertrophy. Meixner stated that this is an important observation because it indicates that the enlargement is not of recent origin or due to a postmortem change. The interstitial tissue between the muscles is increased. The question has frequently arisen whether this increase in connective tissue is due to a slow interstitial inflammation or whether it occurs incidentally during cardiac enlargement.

In the hearts collected by Meixner histologic examination showed an increase of connective tissue between the muscle bundles, as well as an increase of interstitial tissue between the individual muscle fibers. The endocardium in some of the hearts was thickened, showing an increase of connective tissue.

It is interesting to notice Meixner's comment on the cause of death in the 11 children. He does not believe that death was due to cardiac failure in any of his patients. Most of the sudden deaths, even in cases of cardiac disease, result from cerebral circulatory disturbances, and some result from metabolic causes, with edema and anasarca. All the 11 children whose cases Meixner described and who came to autopsy died suddenly. Six had convulsions, and 1 died during convulsions. In other cases he found catarrhal inflammation of the respiratory tract,

29. Richter, M.: Gerichtsärztliche Diagnostik und Technik, Leipzig, S. Hirzel, 1905, p. 121, footnotes.

30. Kolisko, A., in Dittrich, P.: Handbuch der gerichtsärztlichen Sachverständigen Tätigkeit, Berlin, Urban & Schwarzenberg, 1913.

sometimes slight lesions of the intestinal mucosa or foci of bronchopneumonia. In not a few instances the infants, as well as the older children, showed an enlarged and firm spleen, and sometimes the liver was enlarged.

So far as the fate of a rachitic child with an enlarged left ventricle is concerned little is known, though Richter suggested that in those who survive hypertrophy of the left ventricle may continue into adult life, because he found in the clinic and at autopsy a similar cardiac change without any other explanation. Meixner found the condition in an 11 year old boy and in a 17 year old boy, with hypertrophy of the left ventricle and with evidence of residual rickets.

From the foregoing review it is evident that Meixner attempted to establish the hypothesis, based on a series of his own observations, that hypertrophy of the left ventricle may be observed in rickets. One recalls that previous observers recorded enlargement of the right ventricle in rickets. This lack of agreement leads to confusion and requires further explanation. Why the enlargement of the left ventricle should be the preponderant lesion in rickets was not stated by Meixner, and if this condition actually occurs in a considerable number of rachitic children one is still in the dark as to the mechanism of its production. In conclusion one may ask what the relationship is between cardiac enlargement and vitamin D deficiency.

In this review I have referred to the literature which treats of the cardiac changes, principally hypertrophy and dilatation in infantile beriberi, scurvy and rickets. It is evident that in the cases of beriberi and scurvy the presence of cardiac enlargement is corroborated by pathologic and clinical evidence. In rickets cardiac enlargement, if it is of general occurrence, has escaped the attention of most astute clinicians. Consequently, in the case of rickets it will be necessary to collect more clinical and pathologic data and offer a more rational explanation of hypertrophy of the left ventricle.

Pediatric Biographies

HARALD HIRSCHSPRUNG

1830–1916

A NOTE ON THE HISTORY OF HYPERTROPHY OF THE COLON

JOHN RUHRÄH, M.D.†

BALTIMORE

Harald Hirschsprung was born in Copenhagen, Denmark, on Dec. 14, 1830, and died on April 11, 1916. He passed his state examination in 1855 and was made a teacher officially in 1861; in 1870 he was made the head physician to the Queen Louise Children's Hospital in Copenhagen. He became professor of diseases of children in 1877. In 1904 he retired from his hospital and teaching positions. On his seventieth birthday there was a celebration in his honor, and a marble bust was unveiled in the hospital. His dissertation was on the occlusion of the esophagus and the small intestines, and later he published many articles on all sorts of subjects pertaining to pediatrics, especially on intussusception, acute rickets, rheumatic nodules and constipation in the newborn infant from hypertrophy of the colon. His paper on this subject appeared in the *Jahrbuch für Kinderheilkunde*.[1]

Hirschsprung's name is usually associated with this disease, perhaps on account of his having given a more convincing account of it than his predecessors, as may be seen by referring to the bibliographies by Finney,[2] Patel[3] and Porter and Weeks.[4] Parry described a case of this condition which is recorded in his collected papers in 1825. His patient was a Dr. C., who was seen in 1804. His age is not given. At autopsy "the dilatation of the colon extended to about the beginning of the sigmoid flexure, where it resumed its normal size." Billard gave an account of a sclerosed colon in a 1 week old baby in his book in 1828, and other early cases were reported by Ebers (1836), von Ammen (1842), Oulmont (1843), Banks, Banfer, Favalli (1846), Little and Galloway (1850), Gay (1854), Henoch (1861), Levitt of Chicago (1867), the first American case, and many others.

† Deceased.

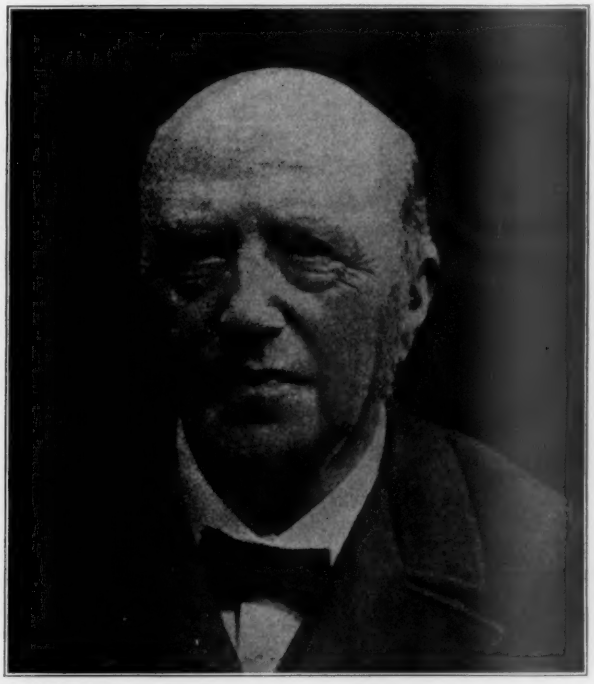
1. Hirschsprung, H.: Jahrb. f. Kinderh. **27**:1, 1887.
2. Finney, J. M. T.: Surg., Gynec. & Obst. **6**:624, 1908.
3. Patel, M.: Toulouse méd. **12**:282, 1910.
4. Porter, L., and Weeks, A.: Megacolon and Microcolon, Am. J. Dis. Child. **9**:283 (April) 1915.

The most important parts of Hirschsprung's contribution are as follows:

CONSTIPATION (STUHLTRÄGHEIT) IN THE NEWBORN DUE TO DILATATION AND HYPERTROPHY OF THE COLON

I permit myself to present to this learned gathering two pathological specimens of an unusual nature, together with short clinical histories, with the hope, through this report, of hearing of similar observations and discussions from the large gathering present.

I will at once present the first specimen. As you see it is colon, but of surprising size considering it is from a child who died at eleven months of age. As



HARALD HIRSCHSPRUNG

the abdomen was opened there appeared a pair of enormously distended coils of intestine, the S. Romanum and the ever still more dilated transverse colon. The rest of the large intestine was enlarged and the rectum was not only dilated but was the seat of a small constriction. The described parts of the intestine are not only distended but the wall markedly thickened in all its layers and particularly in the muscular part. Besides this, the mucous membrane in the less thickened parts shows disseminated erosions and ulcerations which show great differences in size and depth. There are very small superficial erosions and ulcerations, scarcely the size of a pin head, which go through the entire thickness of the mucous membrane. These are discrete, small losses of substance and larger ones which apparently are formed by the coalescing of two or three others, as one

can see small strips of what is left of the mucous membrane passing through the ulcers, and in certain places the surface of the bowel on this account has a meshlike appearance. All the ulcers have a somewhat round or oval form with regular, slightly undermined edges as if hewn out. Here and there one sees fine follicle openings but no swelling of the follicles. There is no trace of inflammation on the serosa. Ligamenta and haustra coli are not recognizable but the appendices epiploicae are strongly developed. The mesentery of sigmoid is high, broad and thickened with rows of hypertrophic, bluish, mesenteric glands up to the size of a bean. In the under part of the ileum Peyer's patches stand out strongly, but in the corpse there are no other changes of importance.

What symptoms did this remarkable disease of the colon cause?

Immediately after the birth of the child, which took place in a lying-in institution in Copenhagen, it showed the peculiarity that in spite of various laxatives it had no stool. Only after repeated enemas did the bowels move. The same sluggish action of the bowel continued in the following months and the various remedies had to be used changing from one to the other, but when it was possible to cause a stool it was of normal consistence and appearance. Otherwise the child was well and thrived on the mother's breast and zwieback gruel.

The child was brought to the policlinic on account of the difficulty of causing defecation. When first seen it had had in the preceding 14 days only small, insignificant small knobby separate movements. Nevertheless the child did not appear to be suffering particularly, and the appetite had remained good. The child had only vomited once. The abdomen was tolerably large but not distended to any considerable degree. In the rectum masses of scybala could be felt, and these were removed partly with the finger and partly by douching. Through the use of various laxatives the condition continued tolerably good, and when the appetite and liveliness began to wane and the color of the skin to become sickly, the child, at the instance of the mother, was taken into the hospital in November, 1880: age 8 months, weight 9,000 grams, nutrition satisfactory. During the entire stay in the hospital, which lasted three months, our entire attention was directed to the relation of the abdomen and the bowel movements. As a rule the child did not have fever, vomited only exceptionally, and had a good appetite; in short the impression was not that of a serious illness. The bowels did not move voluntarily, the abdomen at times was enormously distended, and all our consideration was directed towards making the bowels move. When this happened the abdomen relaxed and the child felt manifestly better. The remissions were, however, of short duration. I confess that I had never known a similar case, neither in the literature nor from my own experience. A constriction of any kind affecting the intestinal canal did not seem under the circumstances possible, or at least not of a permanent character. The fact that a thick, elastic tube, more than an ell in length, as a rule permeable with the greatest ease, and that the rectum by examination was found full of fecal masses, which did not empty spontaneously, argued against a low as well as a high constriction of the intestinal tract and seemed rather to denote an atonic condition of the lower part. But the methods of treatment used in this connection, massage and electricity, were of no avail, but by the daily use of laxatives and injections of water the movements were in a way regulated. The abdomen was seldom distended to any great degree, and the child left the hospital having gained during its stay 700 grams. It stayed home only a short while. During the first eight days the child was right well, and it had spontaneous movements which, contrary to the former habit, were thin. Then the abdomen again became markedly distended, the movements extraordinarily

frequent, then, mustard colored; the boy became suddenly very thin and died the same day he was returned to the hospital. His weight was only 6,900 grams.

A case of illness, like the one communicated, stands as unique. It has always a certain interest, but when one can report others of the same kind it takes on an added significance as cannot be denied—and some years later I saw a similar case.

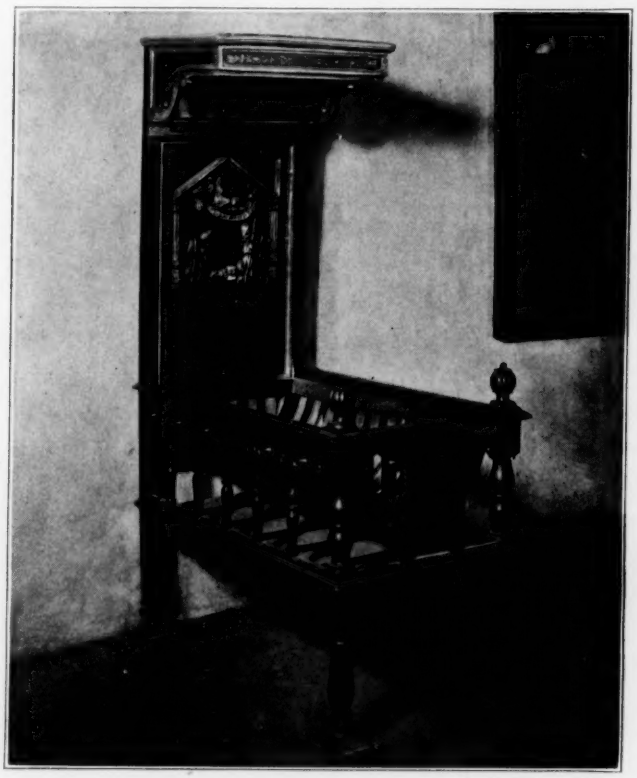
Hirschsprung's paper continues with an account of a case in a boy, aged 7 months, and this is followed by some speculation as to the cause of the condition.

Pediatrics in Art

SIXTEENTH CENTURY CRADLE

JOHN RUHRÄH, M.D.†
BALTIMORE

Cradles go back to the earliest times, and there have been many different designs, chiefly differentiated into those which rock and those which do not. The accompanying illustration shows an excellent example of a cradle which is a fine work of art. It is in the Museo Civica



Sixteenth century cradle; North Italian.

in Saluzzo, one of the towns of Piedmont. The museum was formerly the Palazzo Cavasso, while the cradle came from the Castello dei Lagnasco.

The cradle is carved, and on the back is depicted the Holy Family receiving the blessing of heaven, while below is a design reminiscent of the art of Pompeii. The legend above the Holy Family reads: "Gloria in excelsis et in terra pax." The baldachin at the top does not extend out as far as is sometimes seen, but far enough to serve as a support for the curtains. This form was much in vogue in the Tyrol and in northern Italy.

† Deceased.

News and Comment

GENERAL

American Board of Pediatrics.—The annual meeting of the American Board of Pediatrics was held June 10, 1935, at Atlantic City. Dr. Alfred A. Walker was reappointed by the Section on Pediatrics of the American Medical Association to succeed himself as a member of the corporation. All the directors and officers were reelected.

Following is the new classification of applicants for certification. The changes are based on the experience gained from examination and on the general requirements as adopted by the Advisory Board of Medical Specialties and the Council on Medical Education and Hospitals of the American Medical Association.

Group I.—Physicians who have specialized in pediatrics for more than ten years. Attention is called to the ruling of the board that no applicant will be certified in this group without examination after September 1936. Until this date examination is optional with the board, and all applicants not strictly confining their work to pediatrics must take the examination. After 1943 this group will be abolished.

Group II.—Physicians who have specialized in pediatrics for from seven to ten years. Applicants must submit evidence of at least one year's hospital training and one year's training in a recognized pediatric center and of continued work in some form of pediatric organization or institution. Examination is required. This group will be abolished in 1938.

Group III.—Five years of training after graduation from a class A medical school, comprising one of the following:

A. One year's service in a general hospital with two years' service in a pediatric center plus two years of specialized practice.
B. Three years' service in a pediatric center plus two years' specialized practice or training.
C. Two years' service in a pediatric center plus three years' specialized practice in pediatrics, including continued work in some pediatric activity.
D. One year's service in a general hospital and one year's service in a pediatric center plus three years' experience in the specialized practice of pediatrics including connection with some pediatric activity.

After 1938 the minimum requirements for group III will be as follows:

Graduate of a class A medical school.
One year's intern service in a general hospital.
Two years' service in a pediatric center.
An additional term of two years of specialized study and/or practice.

National Board of Medical Examiners.—At the annual meeting of the National Board of Medical Examiners, held at Atlantic City, it was voted to include pediatrics as one of the subjects in the examination for licensure. One and one-half hours in the written part of the board's examination will be devoted to pediatrics.

UNIVERSITY NEWS

Dr. Katsuji Kato has been promoted to assistant professor of pediatrics in the medical school of the University of Chicago.

CORRECTION

In the article by J. A. Johnston and John W. Maroney, entitled "Carbohydrate Metabolism: III. Relation of Salt and Water to the Oxidation of Dextrose," in the May issue (Am. J. Dis. Child. **49**:1240, 1935), the last word in the caption for table 5, on page 1251, should read "Dextrose" instead of "Water."

Abstracts from Current Literature

Pathology, Bacteriology & Biochemistry

THE EFFECT OF THE THYROTROPIC HORMONE ON AUTO- AND HOMEOTRANSPLANTS OF THE THYROID AND ITS BEARING ON THE QUESTION OF SECRETORY NERVES. DAVID MARINE and S. H. ROSEN, Am. J. Physiol. **107**:677 (March) 1934.

The thyrotropic hormone of the anterior lobe of the pituitary produced hypertrophy of thyroid transplants to the same degree as of the nontransplanted thyroid. This reaction is brought about by stimulation of the thyroid cells through the blood stream.

NOURSE, Cleveland.

BACTERIAL ACTIVITY IN DIFFERENT LEVELS OF THE INTESTINE AND IN ISOLATED SEGMENTS OF SMALL AND LARGE BOWEL IN MONKEYS AND IN DOGS. G. M. DACK and ELIZABETH PETRAN, J. Infect. Dis. **54**:204 (March-April) 1934.

Dack and Petran present some fundamental studies on bacterial activity in the intestine. The details are too numerous to abstract, and the article is worthy of careful perusal. In general, they conclude that gastric acidity is not a constant barrier to the entrance of organisms into the gastro-intestinal tract; that the contents of the small intestines are not bactericidal, as is now generally held; that peristalsis and secretions play an important part in rapidly freeing the small intestines from organisms, and that the colon bacillus is primarily adapted to grow and to remain viable in the mucous secretions of the empty large bowel.

TOOMEY, Cleveland.

THE FILTRABILITY OF THE ACID-FAST GROUP. FRANK B. COOPER, J. Infect. Dis. **54**:236 (March-April) 1934.

Cooper, working with Mycobacterium phlei, was unable to obtain growths from any filtrate, regardless of culture conditions.

TOOMEY, Cleveland.

POSTURAL DEFORMITIES AND BONE GROWTH. A. B. APPLETON, Lancet **1**:451 (March 3) 1934.

This is the report of an experimental investigation of the effects of postural deformity on the bones and muscles in a series of healthy rabbits. The postural deformities were brought about by the application of splints or section of or interference with the nerve supply of some single muscle or group of muscles.

These experiments have shown that changes in the form of healthy bones result from the adoption of unusual postures in growing animals, but no changes could be recognized in adult animals.

LANGMANN, New York.

NEPHRITIS WITH ACIDOSIS, ALBUMINURIA AND SEROUS EXUDATION PRODUCED IN RABBITS BY THE INJECTION OF STREPTOCOCCIC FILTRATES. PASTEUR VALLERY-RADOT, MAURICE DÉROT and P. GAUTHIER-VILLARS, Compt. rend. Soc. de biol. **113**:582, 1933.

Hemolytic streptococcic filtrate in doses of 0.25, 1.5 and 0.33 cc. per kilogram of body weight was injected into forty-one rabbits on sucessive days. Twenty-one of the animals survived and recovered from the shock, and within a variable number of days, usually the sixth day or a little later, albumin appeared in the urine. The resulting edema was occasionally peripheral or even in the serous cavities.

The uric acid in the blood increased in nineteen of the twenty-one animals. When the animals were killed and studied pathologically, acute glomerular changes and slight diffuse interstitial changes with practically no tubular abnormalities were seen.

WAHL, Cleveland.

MODIFICATIONS OF BLOOD CALCIUM FRACTIONS FOLLOWING ADMINISTRATION OF PARATHYROID HORMONE. A. CABITTO, Clin. pediat. **16**:221 (March) 1934.

When parathyroid hormone increases the total calcium there is conversion of the colloidal calcium into ultrafiltrable calcium; and, conversely, there is conversion of ultrafiltrable calcium into colloidal calcium when there is a diminution of total calcium. Cabitto experimented on dogs.

DOOLEY, New York.

STUDY ON CHLORINE ENRICHMENT IN YOUNG DOGS. G. TÖRÖK and L. NEUFELD, Arch. f. Kinderh. **102**:37 (April 27) 1934.

Young dogs were fed high sodium chloride diets, and the internal organs were analyzed for the amount of chloride stored. In the dogs made ill by the high intake of sodium chloride, the liver, muscles and brain showed an increased sodium chloride content, but the skin and lungs contained less sodium chloride than in the control dogs. The dogs which developed well and thrived on the high intake of sodium chloride showed slightly greater values for sodium chloride in the liver, muscles and brain than the dogs which were not given additional sodium chloride.

LEMASTER, Evanston, Ill.

INFLUENCE OF GASTRIC JUICE ON THE BLOOD BUILDING OF RATS. JOHANNA ENGBERDING, Monatschr. f. Kinderh. **59**:332, 1934.

Engberding's work is based on the observations of Castle and those of Morris, who showed that in pernicious anemia reticulocytes can be increased by the feeding of raw meat which has been digested by normal gastric juice. Engberding's studies were designed to determine whether the normal gastric juice of children contains such a blood-building substance. Not having any patients with pernicious anemia, she carried out her experiments on rats. The work was rather extensive, the rats being divided into different groups according to their weight and also segregated as regards their diet. One group received milk and bread, and the other meat and vegetables. Later a special vitamin-free diet was devised. The results were greatly confused by the fact that all the animals seemed to react with an increase in reticulocytes when blood was withdrawn. These reactions were so confusing that Engberding concludes that rats are not adapted to experiments on the determination of anti-anemic substances in gastric juice.

GERSTLEY, Chicago.

THE SPECIFIC GRAVITY OF THE ERYTHROCYTES. G. A. LINDEBOOM, Acta med. Scandinav. **81**:415 (April 14) 1934.

An interesting fact observed by Lindeboom was that the specific gravity of the whole blood is from 1.058 to 1.061 in normal males, while it is from 1.056 to 1.059 in females. The specific gravity of the plasma and red blood cells is identical in both sexes. Only when the color index is very abnormal does the specific gravity of the erythrocytes differ from the normal; there is no strict parallel relation between these two values. The rate of sedimentation is increased when the specific gravity of the red blood cells is increased.

LASLO KAJDI, Baltimore.

THE COAGULATION OF BLOOD. F. LEIRI, Acta med. Scandinav. **82**:268 (May 24) 1934.

The circulating blood produces a current potential, which imparts a positive charge to the dispersive medium of the plasma, while the protein particles are negatively charged. Of the different protein fractions the fibrinogen is nearest its

iso-electric point. In shed blood or in injured blood vessels, if circulation ceases or becomes very slow, this positive charge is dissipated, and fibrinogen precipitates around the fragments of the disintegrated platelets as *germes de coagulation.* Leiri questions the existence of the thrombokinase. KAJDI, Baltimore.

Nutrition

THE HEART VALVES AND MUSCLE IN EXPERIMENTAL SCURVY WITH SUPERIMPOSED INFECTION, WITH NOTES ON THE SIMILARITY OF THE LESIONS TO THOSE OF RHEUMATIC FEVER. JAMES F. RINEHART and STACY R. METTIER, Am. J. Path. **10**:61 (Jan.) 1934.

In guinea-pigs scurvy causes atrophy and degeneration of the collagenous stroma of the valves of the heart. In guinea-pigs fed an adequate diet infection produces no significant lesion in the valves of the heart. In scurvy with added infection there are degenerative and proliferative changes in the valves of the heart similar to those in acute rheumatic fever. It is suggested that a condition of vitamin C deficiency may be a necessary background for the development of rheumatic fever.

MOORE, New York.

THE CLINICAL ASPECTS OF CHILD FEEDING. PHILIP S. POTTER, Arch. Pediat. **51**:148 (March) 1934.

Potter points out in some detail the part played in body economy by the various food elements, mineral salts and vitamins. The matter of particular foods, their preparation and other aspects are considered in detail, with Potter's interpretation of when and how these foods should be used. Undoubtedly this article will seem extremely conservative to many of the present day pediatricians.

WADDELL JR., University, Va.

ON THE ALLEGED TOXICITY OF COD LIVER OIL. WARREN M. COX JR. and ALLAN J. ROOS, Bull. Johns Hopkins Hosp. **54**:430 (June) 1934.

Cox and Roos review the literature (experimental and clinical) on the toxic effects of cod liver oil. They were especially interested in cardiac damage. Rats were used in the experiments. The diet was adequate but contained 27.3 Gm. of cod liver oil per kilogram of body weight (78 per cent of the calories). The rate of growth was subnormal, and other deleterious effects were observed, but there was no histologic evidence of any pathologic lesion in the heart.

LYTTLE, New York.

FLUID DISTRIBUTION AND EDEMA. A. ASHLEY WEECH, Bull. New York Acad. Med. **10**:269 (May) 1934.

The regulation of the distribution of fluid in the body depends on the following:

(*a*) Factors operating at the wall of the capillary. These include the colloid osmotic pressure of the plasma, the capillary blood pressure, the colloid osmotic pressure of tissue fluid, the mechanical pressure in the tissue spaces and the permeability of the capillary wall.

(*b*) Factors which modify the forces on the outside of the wall of the capillary. Here one deals with the flow of lymph and the elasticity of the tissues.

(*c*) Factors which modify the forces or the inside of the wall of the capillary and which depend on excessive proteinuria, protein starvation, venous obstruction and cardiac stasis, variations in the intake of salt and the kidney.

There is a comprehensive discussion of each of these factors from the biochemical as well as from the clinical point of view. Experimental and clinical data are presented to illustrate each mechanism involved. JAHR, Omaha.

A Clinical Method for Determining Moderate Degrees of Vitamin A Deficiency. P. C. Jeans and Z. Zentmire, J. A. M. A. **102**:892 (March 24) 1934.

The usual recognized clinical evidences of vitamin A deficiency are associated only with marked degrees of deprivation of vitamin A, of which night blindness is one. A routine test for night blindness probably would reveal many more cases than are now suspected. Jeans and Zentmire show that the visual tests employed in their study constitute a satisfactory means for determining mild degrees of vitamin A deficiency. The method is described. Application of this test for determining the sensitivity to light following partial dark adaptation in two hundred and thirteen children showed that forty-five had subnormal dark adaptation. Twenty-one of these were kept under observation and given a good diet that included cod liver oil. All these regained normal adaptation. The average period of recovery was twelve days. Jeans and Zentmire believe that this is a satisfactory test for detecting moderate degrees of vitamin A deficiency.

Bonar, Salt Lake City.

Obesity in Children. Norman K. Nixon, J. Pediat. **4**:295 (March) 1934.

The general problem of obesity in children is discussed. The metabolism of fat and the various theories concernng the etiology of obesity are considered. Recent evidence suggests that the nervous system plays a more important rôle in fat regulation than the endocrine glands. The treatment of obesity in children consists essentially in lowered caloric intake and increased muscular activity. At times thyroid substance given by mouth is of value. Other glandular products have proved disappointing in most cases.

LeMaster, Evanston, Ill.

Insulin in Undernourished Nondiabetic Children. Leo S. Radwin and Samuel S. Brown, J. Pediat. **4**:315 (March) 1934.

Injections of insulin were given to nondiabetic boys who were moderately undernourished, in an attempt to cause an increase in body weight.

There was no increase in the rate of gain when less than 10 units of insulin was given twice daily. Fifteen units given twice daily caused a slight increase in the body weight, which was lost within a month after the insulin was discontinued.

Reactions to insulin were not infrequent. Radwin and Brown advise against the use of insulin in undernourished, nondiabetic children.

LeMaster, Evanston, Ill.

The Effect of Cooking on the Digestibility of Cereals. John R. Ross and Lida M. Burrill, J. Pediat. **4**:654 (May) 1934.

Cooking for more than thirty minutes in a double boiler did not significantly increase the digestibility of cereal starches under standard conditions in vitro. The following cereals showed about the same rate of digestion of starch: Cream of Wheat, corn-meal, Mead's Cereal, Quaker Rolled Oats, and Quick Quaker Oats. The digestion of the starch of Pablum was more rapid and more complete than that of any other cereal.

LeMaster, Evanston, Ill.

Milk-Free Diet in Pyuria and Eczema of Children. A. Mader, Indian J. Pediat. **1**:99 (Jan.) 1934.

The composition of most of the vegetable proteins is such that they are not adequate for the development of the growing organism. An exception to this is soy-bean, which contains the biologically important amino-acids lysine, tryptophan and cystine. An additional advantage of soy-bean consists in its being a soluble saccharose and containing a high percentage of lipoids and minerals. The soy-bean

diet prepared by Mader's special method (*Soyabasan*) makes the urine strongly alkaline, with a p_H between 8.2 and 8.4. This is due to the high content of bases in soy-bean flour. Used for its alkalizing effect in ordinary pyuria, the soy-bean diet has entirely replaced other methods of treatment (such as that with methenamine and phenyl salicylate) in Mader's clinic. In the dietetic treatment of eczema the soy-bean diet is highly effective because of the high mineral content and the change of metabolism toward the alkaline side. In eczema good local results are obtained with an ointment which contains an irradiated cholesterol. In strongly itching types of eczema and neurodermatitis suprarenal hormone given in doses of from 0.2 to 0.3 cc. at intervals of five days is very effective through its regulation of calcium metabolism.

GONCE, Madison, Wis.

GASTRIC DIGESTION OF RAW AND BOILED MILK IN INFANTS. JESSIE W. OGILVIE and OLIVE D. PEDEN, Lancet **2**:76 (July 14) 1934.

In carrying out this study the gastric contents were removed before and at half-hour intervals after test feeding of raw and boiled milk. The following were used as indexes of the course of digestion:

1. The amount of free hydrochloric acid and total chlorine and the degree of total acidity.

2. The peptic activity, to determine whether any change in the physicochemical composition of the milk alters the secretory activity of the zymogen glands.

3. The amount of soluble nonprotein nitrogen, as an index of the extent to which proteins are disintegrated.

4. The amount of soluble calcium, as an indication of the capacity of the gastric secretion to convert minerals into a soluble and therefore readily assimilable form.

Ogilvie and Peden conclude from their study that there is no significant difference in the gastric digestion of boiled and raw milk and therefore that milk is not adversely affected by boiling.

LANGMANN, New York.

IDIOPATHIC STEATORRHEA, TROPICAL AND NONTROPICAL SPRUE AND INTESTINAL INFANTILISM. E. HESS THAYSEN, Arch. d. mal. de l'app. digestif **24**:123 (Jan.) 1934.

Thaysen asserts his belief that celiac disease and sprue are identical rather than distinct pathologic entities. Tropical sprue, nontropical sprue and intestinal infantilism are discussed from the point of view of symptomatology, aphthous stomatitis, anemia, achylia, nervous symptoms, articular pains, osteoporosis, the endocrine glands, the glycemic curves, the basal metabolism, the etiology and the pathogenesis. Thaysen concludes that, granting that the etiology of the three conditions is unknown, it seems probable that, so far as the onset, evolution, symptomatology, pathologic anatomy and perhaps also the pathogenesis are concerned, they are identical. He proposes to group them under the name "idiopathic steatorrheas."

TURNER, Chicago.

THE FRUIT REGIMEN IN INFANTILE FORMS OF DIARRHEA. M. SCHACHTER, Arch. de méd. d. enf. **37**:139 (March) 1934.

In 1928, Heisler, a practicing physician of Königsfeld, in a rather elaborate brochure proposed the revival of the somewhat ancient German custom of treating dyspeptic conditions of childhood with an apple dietary. The use of apples in the management of diarrheal disorders of infancy was later placed on a scientific basis by Moro of Heidelberg and was discussed at the International Congress of Pediatrics at Stockholm in 1930. At first this theory seems in direct contradiction to all known conceptions of proper diet in enteric diseases of early life, every author insisting on as complete rest as possible for the digestive tube. As a matter of fact, Moro and Heisler recommend the administration of adequate quantities of water alone for the first two or three days; purée of apple is then

offered in amounts of not more than from 100 to 300 Gm. at a feeding and not more than 1,500 Gm. per day; no special choice of apples is necessary, but these investigators insist that they must be fully ripe. Several days of treatment seems sufficient in most cases, after which tea, biscuits, purée of potato and other foods may be introduced.

Schachter has obtained excellent results, not only in diarrheas but in celiac disease. In the latter syndrome the use of an apple diet appears to be as salutary as the treatment with banana introduced by Fanconi of Zurich.

AMESSE, Denver.

ALIMENTARY HYGIENE OF INFANCY. G. MOURIQUAND, Bull. Assoc. internat. de pédiat. prevent. **1**:3 (Sept.) 1934.

After many years of observation Mouriquand maintains that in certain deficiency diseases there are agencies which he terms "revealing" factors, which verify these diseases. These may be physiologic, such as gestation, parturition and growth, or pathologic, such as toxic, infectious and meteorological factors. In the former group, the author cites growth as a revealing factor in acute rickets and beriberi and cites many examples to illustrate the complexity of the problem; on the pathologic side he deals particularly with infectious processes and with the various vitamin deficiencies.

AMESSE, Denver.

DIMINUTION OF THE PLASMA POTASSIUM BY ETHER ANESTHESIA. A. D. MARENZI and R. GERSCHMAN, Compt. rend. Soc. de biol. **113**:475 (April 6) 1933.

Marenzi and Gerschman showed in previous articles that the potassium content of the blood is definitely lowered during and following ether, chloroform, a dextrose derivative of chloral and morphine anesthesia.

Owing to controversy with other investigators, the experiment was repeated on dogs with ether anesthesia. It was found that within from one-half to one hour during or following the anesthesia the potassium content dropped about 6 mg., returning to normal within from four to six hours after.

WAHL, Cleveland.

INDICATIONS FOR GAVAGE. B. WEILL-HALLÉ and MARCUS, Nourrisson **22**:90 (March) 1934.

In describing the technic, emphasis is placed on having the baby in the vertical position during the whole period of the gavage and immediately following. Among the more important indications cited are:

1. Disturbances of the nervous system which interfere with sucking and swallowing.
2. Serious anomalies of the lips, maxilla, tongue or palate.
3. The trismus of tetanus neonatorum.
4. Postdiphtheritic paralysis.
5. Anorexia in those acutely ill.
6. Prematurity and congenital debility.
7. Hypothrepsis. In this condition gavage should not be delayed too long.

MCCLELLAND, Cleveland.

DYSTROPHIC LYMPHATISM OF INFANCY AND CHILDHOOD. G. MOURIQUAND, Paris méd. **2**:17 (July 7) 1934.

Under the nomenclature of dystrophic lymphatism, Mouriquand considers that disturbance of nutrition which is characterized by a tendency of the tissues to hold more water than is normal. These children are heavy, pasty and pale, with thick tissues, and tend to have colds and blepharitis. In the older child the resemblance

to a hypothyroid state or to dystrophia adiposa genitalis is often striking, and in such instances glandular therapy is helpful. The condition tends to disappear with adult life, and for this reason the possibility of a hereditary factor is often overlooked. Congenital factors must also be considered, particularly a syphilitic infection. Lack of vitamins and of sufficient proteins, together with overfeeding of carbohydrates, is an important postnatal factor. Therapy consists in proper alimentation and hygiene and the assurance of good climatic conditions.

LESLIE, Evanston, Ill.

EGGS AND CEREAL IN THE DIET. P. NOBÉCOURT, Gaz. d. hôp. **107**:713 (May 16) 1934.

Nobécourt emphasizes the general principles of nutrition in the first few years of life.

Eggs, besides supplying protein and lipoids, are an important source of minerals and vitamins. The author condemns the use of storage eggs for infants. He advocates their cautious addition to the diet at the age of 16 months. Cereals ought to be given daily. Various ways of preparing them are described.

LASLO KAJDI, Baltimore.

QUANTITATIVE VARIATIONS IN THE FAT OF HUMAN MILK AT DIFFERENT TIMES DURING A NURSING. D. LUCIGNANI, Riv. di clin. pediat. **32**:412 (April) 1934.

Lucignani made observations on the percentage of fat in human milk collected at four different times: before the child began nursing and after it had nursed five, ten and fifteen minutes. He recorded the amount of milk the baby consumed in the first, second and third five minutes of the same nursing.

Usually, the percentage of fat in the milk before nursing was about 1.5; it increased after five minutes of nursing, and after ten minutes reached its maximum (from 4 to 10 per cent); it dropped somewhat during the last five minutes of nursing. The quantity of milk taken by the child was greatest in the first five minutes, was much smaller during the second 5 minutes and increased a little in the third five minutes. In general, the child obtained the most milk when the percentage of fat was the lowest and the least milk when the percentage of fat was the highest.

HIGGINS, Boston.

PSYCHIC AND NEUROLOGIC SYNDROME IN RICKETS. M. SCHACHTER, Med. de los niños **35**:101 (April) 1934.

Rickets is a disturbance of the entire organism, not of the bones alone. In infancy sweating appears in few conditions other than rickets. This is evidence of a disturbance of the vegetative nervous system. Schachter quotes many authorities to support his contention that there exists in rickets a substance that produces excitation of the nervous system. Some of the symptoms pointing to this involvement are muscular hypotonia, spasmophilia, catalepsy and hydrocephalus.

There is authoritative evidence that psychic disturbances and disorders of conduct approaching dementia have their origin in florid rickets. Hulschinski of Berlin formulated the theory that the dementia of rickets evolves in three periods: asthenia, catalepsy and finally paranoia.

DWYER, Kansas City, Mo.

NORMAL ALKALI RESERVE IN CHILDREN. C. DE TOMMASO and G. RUFF, Prensa méd. argent. **20**:2689 (Dec. 27) 1933.

The carbon dioxide value varies from 52 to 60 volumes per cent of plasma (average, 56). In the cases studied the apparent acidity per liter was from 101 to 440 cc. of one-tenth normal hydrochloric acid; and the organic acidity, from 312 to 680 cc.

KUGELMASS, New York.

HYDROGEN ION CONCENTRATION OF THE BLOOD. W. BLADERGROEN, Chem. Weekblad **30**:526, 1933.

A critical review of methods for determining the hydrogen ion concentration of the blood indicates that only the electrometric method of Michaelis is trustworthy; the quinhydrone electrode method is not recommended. For a given person the p_H varies between close limits, except under markedly abnormal conditions, such as diabetic coma. Determination of the p_H is usually not as important as determination of the alkali reserve and free carbon dioxide.

KUGELMASS, New York.

BLOOD IODINE VALUES IN HUMAN RICKETS AND TETANY. A. NITSCHKE and H. DOERING, Klin. Wchnschr. **12**:1910 (Dec. 9) 1933.

The blood iodine was found to be approximately 9 micrograms per hundred cubic centimeters in normal children, 3 micrograms in children with extreme rickets and 2.8 micrograms in those with latent or manifest tetany. The basal metabolism was also low. Individual cases varied considerably, but under treatment with vitamin D (viosterol), the blood iodine returned to normal within from ten to twenty days. This is a preliminary report.

KUGELMASS, New York.

RELATION OF LYSOZYME TO A DIET DEFICIENT IN VITAMIN A. MAX FRANK, Monatschr. f. Kinderh. **60**:345, 1934.

Efforts have been made to relate lysozyme in the organs and tissues to vitamin A. Frank, by giving appropriate diets to rats, rendered them deficient in vitamin A. He then determined the lysozyme content of several of the organs and found no change, except in the liver. On the basis of these experiments he suggests that deficiency in vitamin A works not directly but indirectly from injury to the liver. Substances are then produced in the blood which prevent the tissues from absorbing the circulating lysozyme.

GERSTLEY, Chicago.

BLOOD FINDINGS IN VITAMIN A DEFICIENCY. MAX FRANK, Monatschr. f. Kinderh. **60**:350, 1934.

In rats fed diets deficient in vitamin A, as well as in two clinical cases of vitamin A deficiency, the blood showed moderate anemia. In the two clinical cases there was a slight increase in polymorphonuclears; in the rats lymphocytes were diminished. The blood platelet count was unchanged. The most striking finding was a definite delay in the coagulation of the blood and a diminution in the fibrinogen of the plasma.

GERSTLEY, Chicago.

CONSUMPTION OF VITAMIN A IN HUNGARIAN SCHOOL CHILDREN. K. WALTNER, Monatschr. f. Kinderh. **60**:361, 1934.

In an effort to learn the dietary habits of the school children of Hungary, Waltner selected eight institutions, three in the city and five in the country, and obtained a report of 6,770 meals of two hundred and fifty children. He found that the general diet is rather low in vitamin A and believes that this is due to the fact that most of the children eat relatively much more meat than vegetables. He gives three tables showing the vitamin A content of different foods. In spite of the apparent deficiency in this diet the children showed no clinical symptoms. He suggests that either the demand for vitamin A is not as great as was formerly believed or that children maintain a considerable reserve supply in the body.

GERSTLEY, Chicago.

IS GLYCOGEN A CONSTITUENT OF URINE? P. JUNKERSDORF and H. MISCHNAT, Ztschr. f. d. ges. exper. Med. **83**:711, 1932.

Neither normal urine nor that in persons with a pathologic condition contains glycogen. The reducing power of normal urine is due to uric acid, purine sub-

stances, creatinine, dyes and derivatives of glycuronic acid; that of the urine in disease is due to sugar, homogentisic acid, hydroquinone, bile acids and other substances.

KUGELMASS, New York.

THE INFLUENCE OF FOODS ON THE FECUNDITY OF MUSCA DOMESTICA. HARUJIRO KOBAYASHI, Keijo J. Med. **5**:35 (March 31) 1934.

This report deals with the results obtained over a period of two years in feeding various foods to more than two thousand lots of flies. The development of the ovaries of the flies, their egg-laying ability and the longevity of the flies were the chief points of the attention. It was found that the adult fly needs saccharose or soluble starch to insure longevity and protein or peptone for maturation of the ovary. Comparing the several varieties of food for the flies, it appeared that biscuit plus peptone was the most favorable food for longevity and for development of the ovary.

LEMASTER, Evanston, Ill.

LEVEL OF THE BASAL METABOLISM AS RELATED TO THE COMPOSITION OF THE DIET. M. ODIN and E. WERDINIUS, Acta med. Scandinav. **81**:249 (March 6) 1934.

In a large part of the population subsisting mainly on a diet of milk, flour, potatoes and butter there is, on the whole, a decrease in the basal metabolic rate. The cause of this is in all probability a comparatively low caloric content of the diet, as well as nitrogen deficiency. It has furthermore been found that there is in these cases an increased tolerance of dextrose, epinephrine, pilocarpine and atropine, indicating diminished irritability of the vegetative nervous system as a consequence of the diet. It is hardly justifiable to suspect an endocrine disturbance in the ordinary clinical sense, since there were no other signs of it in any case.

KAJDI, Baltimore.

Prenatal Conditions

CONGENITAL ATRESIA OF THE ESOPHAGUS. R. H. MCCLELLAN and THEODORE O. ELTERICH, Arch. Pediat. **51**:171 (March) 1934.

Two cases of this condition are reported.

WADDELL JR., University, Va.

CLEIDOCRANIAL DYSOSTOSIS. WILLIAM C. COOK, Arch. Pediat. **51**:183 (March) 1934.

Cook reports a case of cleidocranial dysostosis diagnosed in a patient 4 years of age. Physical examination showed brachycephalia, with a well marked depression along the suture lines and over the fontanels. The shoulders appeared more rounded than normal, and on palpation neither clavicle could be felt. There was no evidence of a high palatal arch or of dental irregularities.

Roentgenograms of the chest and skull confirmed the diagnosis. A roentgenogram of the chest showed absence of both clavicles, and stereoroentgenograms of the skull showed the wide sutures and wide fontanels.

WADDELL JR., University, Va.

HEREDITARY SCOLIOSIS. HUGH G. GARLAND, Brit. M. J. **1**:328 (Feb. 24) 1934.

Garland discusses briefly the hereditary factors in scoliosis, which he states are in accordance with the mendelian law. A brief description of the usual deformities of this condition follows, and a family is described in which there has been scoliosis in five consecutive generations. Garland claims that the condition is a mendelian dominant.

ROYSTER, University, Va.

DOLICHOCOLON AND MEGACOLON IN THE INFANT. P. NOBÉCOURT and ROBERT RICHARD, Arch. de méd. d. enf. **37**:193 (April) 1934.

Seven cases of these developmental disorders, either distinct or combined, are reported in considerable detail, with a discussion of the embryology, physical signs and symptoms. The roentgenographic illustrations in this excellent review are unusually complete and satisfactory.

AMESSE, Denver.

A CASE OF HERMAPHRODITISM. L. OMBRÉDANNE, Progrès méd., Aug. 11, 1934, p. 1274.

A child of 8 years, presenting a masculine type of somatic development, showed the following combination of genito-urinary abnormalities: The penis was well developed but did not contain the urethra, which presented its opening below the penis. No testicles and no vagina were present, but abdominal exploration revealed a well formed uterus, fallopian tubes and ovaries. The question of the future of the child is thoroughly considered. The condition is probably associated with an adrenal tumor, and malignant evolution may cause death before a decision as to sex is imperative. Ombrédanne believes that the child should be considered a male because of the type of somatic development and the unsatisfactory results obtained in attempting to construct an artificial vagina.

LESLIE, Evanston, Ill.

AN UNUSUAL CASE OF CONGENITAL CYSTIC LYMPHANGIOMA. R. BUCHER, Deutsche Ztschr. f. Chir. **243**:161 (April 7) 1934.

A girl delivered at term died during labor. Large cystic lymphangiomas were present, involving both arms and the thorax. These are well shown in a photograph of the infant. The postmortem observations, histologic appearance of the tissues and the literature on the subject are discussed in great detail.

GLASER, Rochester, N. Y.

PERIODIC BREATHING IN PREMATURE INFANTS. C. E. RÄIHÄ and T. SALMI, Acta pædiat. **15**:198 (March 28) 1934.

Periodic respiration is so usual in premature infants that it may be termed physiologic. The explanation of the phenomenon is uncertain. Although it is generally assumed that it depends on the incomplete state of expansion of the pulmonary alveoli, Ylppö conceded only a minor rôle to this factor and emphasized the importance of the abnormally acid reaction of the blood and tissues of premature infants. He admitted that in some instances the condition is due to the presence of intracranial hemorrhage. Other authors have stressed the mechanical inefficiency and physical weakness of the thorax in immature infants; still others have concentrated their attention on underdevelopment of the regulatory function of the central nervous system. Salmi believes that the respiratory irregularity of both premature infants and new-born infants born at full term results from both central and peripheral peculiarities. Among these, fatigue of the respiratory musculature is important. He concurs in the opinion of others that young infants exhibit a constant state of marked hyperpnea.

A priori one would expect the respiratory pattern both of premature infants and of new-born infants born at full term to be influenced by the high concentration of hemoglobin in their circulating blood and also by their relatively low basal metabolic rate. The investigations of Haldane and Douglas dealing with periodic breathing following forced hyperpnea find suggestive application in this connection.

Räihä and Salmi report the results of their study of the relationship between the concentration of hemoglobin in the blood and the presence of periodic breathing in seven premature infants. All had high hemoglobin values during the neonatal period, and all showed periodic respiration. As the concentration of hemoglobin fell to normal or below normal their breathing became more regular. The transition was gradual, and no threshold could be determined for its occurrence. In two

litters of new-born rabbits anemia was produced quickly by bleeding; a rapid change from periodic to regular breathing took place. Three normal rabbits were made plethoric by giving them transfusions of properly matched homologous blood; as the hemoglobin concentration rose the respiratory rhythm showed well marked periodicity. In these experiments neither shock nor circulatory embarrassment was apparent.

The authors feel some hesitancy in offering a physiologic explanation for this neat parallelism. They advance a tentative hypothesis which correlates their data with those of other investigators. In this hypothesis the anatomic and functional immaturity of the capillary system in premature infants is given a place of importance.

McCune, New York.

Acute Infections

Atabrine and the Treatment of Malaria in the Philippine Islands. P. E. McNabb and S. C. Schwartz, Am. J. Trop. Med. **14**:309 (July) 1934.

McNabb and Schwartz review briefly the literature on the treatment of malaria with atabrine and report their results with this drug in treating fourteen patients with malaria in the Philippine Islands. One case of blackwater fever is reported in detail. They concluded that atabrine gives excellent results in both malignant and benign tertian malaria, and that a five day course of treatment is just as effective as a seven day course. No toxic effects were noted, and no known relapses occurred in from four to ten months following the treatment.

Burpee, Augusta, Ga.

Plasmodium Falciparum Welch, 1897: Does Direct Division of the Parasites Precede Schizogony? Hans E. Hingst, Am. J. Trop. Med. **14**:325 (July) 1934.

Hingst briefly reviews the literature on the direct division of the malaria parasite Plasmodium falciparum. He subscribes to the theory of direct division of Plasmodium falciparum as being one method of multiplication and advances certain photomicrographic evidence in proof of this theory. He believes also that multiplication takes place by schizogony, and that the two methods probably account for the variations in the estivo-autumnal cycle.

Burpee, Augusta, Ga.

Encephalomyelitis Following Measles. A. M. McCausland and S. J. McClendon, Arch. Pediat. **51**:178 (March) 1934.

A case of encephalomyelitis in a child 3 years of age is reported. On the eighth day of an attack of measles the child had a sudden convulsive attack, followed by coma. This was associated with protracted vomiting and inability to swallow. Changes in the eyegrounds, papilledema and abnormality of the reflexes occurred. The spinal fluid was sterile and showed no increase in cells. Gradual recovery took place. The encephalogram and the clinical course indicated that future mental and nervous systemic manifestations would be slight, even though most patients with this conditon have residual symptoms. The encephalogram was a distinct aid in ruling out certain other definite conditions, such as tumor of the brain and hydrocephalus, and the procedure may also have been of therapeutic value.

Authors' Summary.

The Treatment of Erysipelas in Children. L. M. Nightingale and S. Starr, J. A. M. A. **102**:761 (March 10) 1934.

Erysipelas is a dread disease in infancy, the mortality rate remaining well over 50 per cent. When local treatment is used from 60 to 90 per cent of the

patients die, and when serum is used the mortality rate is decreased to from 40 to 60 per cent. Scattered reports of the efficacy of ultraviolet therapy in erysipelas have appeared. The present article deals with this method of treatment. Nightingale and Starr believe that ultraviolet therapy has so far been most successful, giving better results than serum therapy. It is less harmful and expensive than the latter. They conclude that this method of treatment should be placed above serum therapy in the treatment of erysipelas. BONAR, Salt Lake City.

STUDY OF THE TREATMENT IN ACUTE TETANUS. F. W. TAYLOR, J. A. M. A. **102**:895 (March 24) 1934.

The results of treatment of active tetanus are unsatisfactory. The specific treatment with tetanus antitoxin, regardless of the route of administration or the amount given, has been ineffective in reducing the mortality. Taylor emphasizes several phases in the treatment of active tetanus that are not generally appreciated. Treatment should be directed along three well defined lines: (1) adequate care of the local wound, (2) the use of sedatives and general care and (3) the administration of tetanus antitoxin—an inseparable triad. If emphasis is to be placed anywhere it should be on sedatives and the local focus. Immediate excision, when possible, or complete exposure and search for foreign bodies should be done under general anesthesia. A foreign body should be suspected until its absence has been proved. The local wound of acute tetanus is a surgical emergency and should be treated as such. Since patients with tetanus die from their symptoms and not from the disease, adequate sedation is imperative. Such preparations as tribromethanol or sodium amytal should be used to maintain light narcosis continuously rather than waiting for rigidity to appear. Particular attention must be given to the maintenance of the fluid intake. As a prophylactic tetanus antitoxin enjoys a high reputation, but in active tetanus it is by no means a specific. It cannot withdraw toxin united with the nervous tissue; it can only neutralize uncombined toxin and it is of value only in preventing active tetanus or lengthening the incubation period. The intramuscular injection of from 30,000 to 60,000 units, possibly repeated in protracted cases, would seem sufficient. The conclusion of two workers forty years ago that "an ounce of clean surgery is worth several pounds of serum therapy" is pertinent.

BONAR, Salt Lake City.

STUDIES ON THE SPECIFICITY OF THE INACTIVATION OF POLIOMYELITIS VIRUS BY SERUM. CLAUS W. JUNGEBLUT, J. Bact. **27**:81 (Jan.) 1934.

A number of antivirus, antibacterial and antitoxic immune serums from either the rabbit or the horse were studied by the author for their capacity to inactivate the virus of poliomyelitis (Aycock passage strain) in vitro. The technic consisted of injecting intracerebrally into monkeys a mixture of 0.2 cc. of a 10 per cent suspension of virus and 0.8 cc. of the various antiserums after this was incubated one and one-half hours at 37 C. and kept in the icebox over night. The virus of poliomyelitis, when tested against antiserums produced by immunization with other neurotropic viruses, such as the virus of herpes, rabies and neurovaccinia, exhibited strict immunologic specificity in that no cross-neutralization occurred. Likewise, the virus of poliomyelitis was not inactivated in vitro by agglutinating antidiphtheria, antipneumococcus and antimeningococcus serums. Among the antitoxic type of immune serums, botulinus, tetanus, and dysentery antitoxic serums failed to inactivate the virus in vitro. Inactivation occurred, however, with three of six samples of antitoxic diphtheria serum and with one sample each of antitoxic scarlet fever streptococcic serum and anticrotalus serum. Further experiments demonstrated that four of fifteen serums obtained from rhesus monkeys after immunization with toxin-antitoxin or toxoid had acquired virucidal properties which were not demonstrable before the beginning of immunization.

STOESSER, Minneapolis.

PARALYTIC ACCIDENTS OF ANTI-RABIC TREATMENT. C. E. KIELY, J. Med. **15**:68 (April) 1934.

An instance of paralysis of the leg, abdominal muscles, bladder and rectum following inoculation against rabies which was apparently due to the treatment and not to the rabies is reported. The paralytic syndrome appeared on the thirteenth day of treatment. The patient had been exposed to but not bitten by a rabid dog. Recovery was slow but essentially complete. The literature is reviewed. The cause of the paralysis is not apparent. The pathologic changes in the central nervous system were similar to those observed in postvaccinal encephalitis. Paralytic accidents following prophylactic treatment are not frequent. Remlinger, in 1927, found 329 instances among 1,164,264 treated persons, less than 2 per cent of whom were under 10 years of age. The mortality was 16 per cent in the affected persons. The clinical symptoms are of three forms: (1) the Landry type of paralysis, with a mortality of 30 per cent; (2) the dorsolumbar myelitic type, with a mortality of 5 per cent, and (3) the monosymptomatic type, with no mortality. Decubitus and cystitis with generalized septicemia are frequently the cause of death. Recovery is usually complete (in 98 per cent of the cases). The intensity of prophylactic treatment seems to bear a positive relation to frequency of recovery. Treatment of the attack is symptomatic. NELSON, Cincinnati.

FULMINATING STREPTOCOCCUS INFECTIONS IN INFANCY AS A CAUSE OF SUDDEN DEATH. SIDNEY FARBER, New England J. Med. **211**:154 (July 26) 1934.

Farber points out that two frequent forms of sudden death in early life are so-called thymic deaths and death from suffocation; that "in the last 2,000 consecutive autopsies at the Boston Children's Hospital we have been unable to find a thymus which we could regard as pathological in size, nor have we found in any case a thymus which has been associated with definite symptoms during the life of the patient. During the past five years we have been able to collect a series of ten instances in which the weight of the thymus lay between 45 and 65 grams. In these cases no symptoms referable to the thymic region were noted during life and in every case an adequate cause for death, not associated with the thymus was found. . . . Cases of true overlying or suffocation from that cause undoubtedly occurred in past years when a heavy mother slept in bed with several children and the new-born baby. The conditions, however, are quite different when a baby is found dead in its own bed or crib, without any evidence of foul play or of accident. . . . The streptococcus hemolyticus is a common cause of fulminating infections in early life. Death may occur within eighteen to forty-eight hours after onset of symptoms. . . . Convulsions, coma, extremely high temperatures and other signs of critical illness are present. The most important findings at autopsy are edema of the brain, spinal cord and optic nerves, early interstitial bronchopneumonia and evidences of damage, secondary to the bacteremia, in the kidneys, liver, spleen and lymph nodes."

GENGENBACH, Denver.

PUBLIC HEALTH REPORT. Pub. Health Rep. **49**:581 (May 11) 1934.

For the four week period ending April 21, 1934, there were 132,389 cases of measles—the highest incidence in recent years. Poliomyelitis showed an increase of 25 per cent over the preceding four weeks. All other contagious diseases showed a low incidence. The general mortality was 12.4 per thousand.

SANFORD, Chicago.

THE EPIDEMIOLOGY OF SCARLET FEVER IN A LANDWARD AREA. JOHN RIDDELL, Brit. M. J. **1**:276 (Feb. 17) 1934.

Riddell gives a résumé of the epidemiology of scarlet fever in the landward area of Stirlingshire during 1921-1930. His findings are summarized as follows:

"1. The periodicity of scarlet fever in this area appears to be one of about five years.

"2. Adults have an annual variation in incidence separate from that of children, and following that of children at about one year's interval.

"3. While the maximum seasonal incidence in children is in October, with a smaller increase in January and February, the maximum in adults is in December and January, with a following increase in March.

"4. The fewer the number of apartments in the house the higher the incidence of fever among children, but the lower among adults.

"5. The smaller the house the earlier the average age of infection among children. This does not appear to be due to overcrowding per se.

"6. Females are more liable to infection with scarlet fever than males, but girls are not affected until a later age than boys, though a larger proportion of their cases come from small apartment houses.

"7. The maximum age of incidence for boys is 5 years, and for girls 6 years."

ROYSTER, University, Va.

CARBON DIOXIDE THERAPY IN LOBAR PNEUMONIA. REGINALD HILTON, Brit. M. J. **1**:418 (March 10) 1934.

This article is an outline of Hilton's experiments to determine whether carbon dioxide mixed with oxygen has any effect on lobar pneumonia so far as its spread and severity or its duration are concerned. Note was also made of the blood pressure, pain and other manifestations. The conclusions are as follows:

"In the absence of respiratory failure, as evinced by shallow breathing, the clinical benefits of CO_2 administration in air are not sufficiently demonstrated by these observations to warrant its routine use in lobar pneumonia."

ROYSTER, University, Va.

A VERY RARE CAUSE OF SUDDEN DEATH. F. A. BELAM, Brit. M. J. **1**:531 (March 24) 1934.

A case of scarlet fever complicated by measles, otitis media and several other minor complications during early convalescence is reported. The child had been up and about and playing during convalescence. She vomited one afternoon and at 5:30 the next morning went into a state of collapse, was unable to lift herself and complained of headache. She was completely conscious; the eyes were normal, and there was no sign of paralysis, but the pulse was imperceptible. She died at 6:05.

Autopsy revealed, among other pathologic changes, acute edema of the brain mostly at the vertex, extending onto the base of the brain and, to a less extent, to the cerebellum. This was supposed to be the cause of death.

ROYSTER, University, Va.

HAEMATOLOGICAL STUDIES IN THE RECENT EPIDEMIC CEREBRO-SPINAL FEVER IN CALCUTTA. C. C. BASU and H. N. CHATTERJEE, Calcutta M. J. **28**:495 (June) 1934.

Hematologic studies were made on twenty-five patients with cerebrospinal fever. The authors conclude that Schilling counts are valuable in making a prognosis. The severity of the infection can be estimated by the increase of nonsegmented forms at the cost of segmented ones. The toxic cell index, obtained by the ratio $\frac{\text{toxic polymorphonuclear cells}}{\text{total polymorphonuclear cells}}$ may also be useful in making the prognosis.

GONCE, Madison, Wis.

EFFECTS OF TONSILLECTOMY ON ANTITOXIC IMMUNITY TO DIPHTHERIA IN A RURAL POPULATION. W. A. BUICE, Lancet **1**:790 (April 14) 1934.

A Schick test was performed on 232 rural children. Of the tonsillectomized subjects, 68 (62 per cent) gave positive Schick reactions. Of those with the tonsils intact, 84 (69 per cent) gave positive reactions. The proportion of positive Schick

reactions among both the tonsillectomized and nontonsillectomized children remained practically on a level through all the age groups. The children, without regard to the factor of tonsillectomy, did not appear to be acquiring immunity to diphtheria as they grew older, which is in contrast with the findings of Zingher and other investigators working among children in large cities.

LANGMANN, New York.

INFECTIOUS PURPURAS COMPLICATING THE COURSE OF ERUPTIVE FEVERS. C. SARROUY, Arch. de méd. d. enf. **37**:456 (Aug.) 1934.

Purpuric types of exanthematous disease in children have been observed since ancient times, the most typical being those associated with smallpox and scarlet fever. This grave hemorrhagic syndrome has been seen much less frequently, however, with measles. Sarrouy reports two such cases from Algiers, the first in an infant whose age is not stated, who recovered after intramuscular injection of the mother's blood, and the second in a child of 17 months suffering from measles, bronchopneumonia and noma, in whom antistreptococcic serum was used. The former patient recovered, and the latter died. Sarrouy calls attention to the tardy appearance of the hemorrhagic eruption in some cases

AMESSE, Denver.

RELATIONSHIP BETWEEN VARICELLA AND HERPES ZOSTER. G. RENARD and P. HALBRON, Arch. d'opht. **51**:151 (March) 1934.

After presenting the arguments for and against the identity of varicella and herpes zoster, Renard and Halbron describe a personal observation which lends support to the hypothesis of a common origin. A boy 6½ years old was admitted to the hospital because of a penetrating wound of the cornea. He was allowed to be up and about the ward as soon as he was well enough. The day after his entrance a man was admitted with typical herpes zoster ophthalmicus. Two days later this man presented an eruption of the skin which it was thought might be varicella or generalized herpes. The boy, eighteen days after his admission, presented typical varicella. No history of varicella in the immediate family or among the neighbors was obtainable. The boy was the only patient of his age in the ward. These observations make it appear that the man with herpes zoster had a herpetic eruption or varicella fourteen days (the normal period of incubation) prior to the development of varicella in the boy.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

A CASE OF MALARIA IN AN INFANT TWO MONTHS OLD. MARIE CAMNER and PROCENCO, Bull. Soc. de pédiat. de Iasi **5**:21 (Jan.-March) 1934.

An infant 2 months old began to have daily chills and fever. A very large, firm spleen was discovered. Malarial parasites were found in the blood. The infant's mother had had daily chills and fever since the eighth month of pregnancy, and malarial parasites had been found in her blood. She had not responded well to quinine by mouth. This case is considered to be one of congenital malaria, in spite of the fact that the placenta appeared normal.

LEMASTER, Evanston, Ill.

PROTEIN AND LIPOID IN THE NONSPECIFIC THERAPY OF INFECTIOUS DISEASES IN INFANCY. F. DE NICOLO, Clin. pediat. **16**:171 (Feb.) 1934.

De Nicolo discusses the nonspecific protein and lipoid therapy in acute infections and records his own experience with a preparation that is rather vaguely described as an extract of nonpathogenic schizomycetes made by Prof. Guiseppe Mezzadroli of the Institute of Experimental Bacteriology. In the sixteen cases reported (ten of typhoid fever, five of pulmonary infection and one of glandular fever) the injection of this material seemed to have favorable results.

DOOLEY, Kent, Conn.

POSTDIPHTHERITIC HEMIPLEGIA AND BULBAR PARALYSIS. ANTONIO CELENTANO, Pediatria **42**:290 (March 1) 1934.

A 6 year old girl one week after the onset of diphtheria exhibited total flaccid hemiplegia on the left side. While the symptoms of hemiplegia were rapidly improving, bulbar paralysis developed, producing death due to paralysis of the respiratory center. Celentano points out that in the treatment of the initial disease (diphtheria) only 2,000 units of serum was administered. He also points out that the adminstration of abundant quantities of serum at the time the bulbar paralysis developed was inefficacious and directs attention to the probability that the direct cause of this fatality was the insufficient amount of serum administered in the early stages of the disease, as well as the inefficiency of even large doses after the paralytic complications had developed.

SIGNORELLI, New Orleans.

GONOCOCCIC INFECTION IN INFANTS. JULIO MARTINEZ PAEZ, Arch. de med. inf. **2**:249 (April-June) 1933.

The gonococcus can affect children at any age. In boys it rarely causes a chronic infection, but in girls the condition is practically always chronic, there being a mixed infection with colon bacilli, staphylococci, and streptococci and other organisms. It must be treated for a long time and at regular intervals. Vaccines and autovaccines are often of some value in chronic cases.

HERRON, Spokane, Wash.

FIGHT AGAINST DIPHTHERIA IN CATALONIA. AUGUST BROSSA BOSQUE, But. Soc. catalana de pediat. **4**:182, 1931.

The mortality and morbidity of this disease are progressively decreasing with the increased use of the generally accepted methods of prophylaxis and treatment.

WATSON, Elmhurst, Ill.

PROPHYLAXIS AGAINST MEASLES. A. STEEGER, Rev. chilena de pediat. **5**:123 (March) 1934.

Steeger recommends the use of convalescent serum. Its effectiveness depends on two factors: the time of injection and the quantity of serum used. If it is used at the beginning of the incubation period only small doses are required. If the period of incubation has advanced or even if invasion by the disease has begun larger doses are required. If the invasion has progressed too far not even a maximum dose will prevent the full development of the disease or modify its course.

Steeger considers the use of convalescent serum of the greatest value in the prophylaxis against measles and advocates its use in every case.

SCHLUTZ, Chicago.

UNDULANT FEVER. CARLOS FLORIANI, Rev. med. de los hosp. **2**:61 (Feb.) 1934.

Floriani gives a complete summary of undulant fever, including the etiology, epidemiology, methods of transmission, pathology, symptomatology, clinical and laboratory findings, differential diagnosis and treatment. He stresses the importance of the prevention of the disease by proper boiling or pasteurization of milk, segregation of the animals, disposal of the excreta and prevention of the deposit of the excreta in public places.

HERRON, Spokane, Wash.

COMPILATION OF RECENT ADVANCES ON THE ETIOLOGY AND PATHOGENESIS OF PERTUSSIS. FRIEDRICH WILDTGRUBE, Ergebn. d. inn. Med. u. Kinderh. **45**: 641, 1933.

Wildtgrube discusses the various views concerning the etiologic relationship of the Bordet-Gengou bacillus to whooping cough. He then describes in some detail the pathologic anatomy and histology of the "pertussis lung and brain," and

refers particularly to the thorough investigations of Pospischill on the pathologic changes in the lungs of patients with whooping cough. He then describes the so-called "basal triangle" and "basal shadows" which Götsche considers positive roentgenologic evidence of pertussis and which Wildtgrube could demonstrate in only twenty-three of one hundred and seven children suffering from whooping cough. He then summarizes his work as follows:

"The Bordet-Gengou bacillus has at present the greatest claim to be looked on as the causative agent of pertussis. Future investigations will decide whether or not another unknown noxa, e. g., a symbion with a filtrable virus, plays a rôle in the causation of the disease. The clinical symptoms of pertussis, the division into stages and the pathologic anatomy are readily explicable on the basis of the pathologic activity of the endotoxins of the Bordet-Gengou bacillus. The invasion of the mucous membranes of the respiratory tract by the Bordet-Gengou bacilli and the biologic processes resulting from their multiplication, lead to catarrhal inflammation which is clinically represented by the catarrhal stage of the disease. As a result of the defensive activities of the tissues, the Bordet-Gengou bacilli are gradually destroyed and dissolved, thus leading to a release of endotoxins. The absorbed endotoxins attack the vasomotor system of the brain or the cerebral tissue itself, as well as the lymphatic apparatus, which leads to the development of the second, or convulsive, stage of pertussis, with the typical paroxysms of coughing and the appearance of a lymphocytosis. The continued dissolution of the Bordet-Gengou bacilli and absorption of the endotoxins explain the exacerbation of the clinical symptoms, which reach their height in the third to the fifth week. At this period the Bordet-Gengou bacilli are no longer demonstrable, but there is an appearance of immune bodies in the blood serum. The first immunobiologic process, i. e. the destruction of the exciting agent, is thus concluded.

"The convulsive stage of pertussis with all its specific respiratory and cerebral symptoms is therefore to be considered as an expression of the injurious effect of the pertussis endotoxins on the respiratory organs and the lymphatic and nervous systems. The degree and extent of this injury, hence the clinical picture, depend on the severity of the intoxication and susceptibility of the corresponding tissues to the organism. The defense mechanism against endotoxins is partly to be found in the development of anti-endotoxins in the blood serum. Clinically, this process is expressed by the gradual cessation of paroxysms of coughing and the decline of other clinical symptoms (declining stage).

"The pathologic manifestations of pure whooping cough, particularly those of the lungs, are further complicated by a secondary infection with other pathogenic organisms (pneumococci, streptococci, influenza bacilli and others). Thus clinical pictures arise in which it is difficult to explain which features are the result of a specific, and which were caused by a secondary, infection. The cause of so-called recurrent whooping cough is to be looked for in the postpertussis persisting morphologic or functional changes of the respiratory organs and the central nervous system, which most often become manifest again through the action of some unspecific irritant."

CAPPER, Philadelphia.

DETERMINATIONS OF BLOOD PROTEIN IN DYSENTERY IN CHILDREN. E. VON FRÖLICH and B. VON GÖZSY, Monatschr. f. Kinderh. **59**:352, 1934.

Determinations were made of the amount of blood protein in cases of dysentery of varying severity. The protein was determined in four fractions, from the finely divided albumin fraction (A fraction) to the much grosser globulin fraction (D fraction). In spite of a considerable amount of work, von Frölich and von Gözsy could not relate the severity of the symptoms in these cases to quantitative changes in the blood proteins.

GERSTLEY, Chicago.

SCARLET FEVER TOXIN: I. TESTING OF THE TOXICITY OF SCARLET FEVER TOXOID BY MEANS OF RABBIT EAR SKIN METHODS. S. NAGATA, J. Orient. Med. **20**: 36 (March) 1934.

Adult rabbits (weighing more than 2 Kg.) usually react to from 0.5 to 1 human skin test dose of scarlet fever toxin. The reaction of rabbit ear to scarlet

fever toxin usually reaches its maximum within from twenty to twenty-four hours, though there are a few cases in which this maximum is reached within forty-eight hours. The susceptibility of rabbit ear skin to scarlet fever toxin shows a local variation, the basal part and thick part of the inner side being more sensitive than the point and outer part of the ear. Rabbit ear skin reacts not only to essential scarlet fever toxin, but also to a concentrated solution of bacterial protein. By the rabbit ear skin method the degree of detoxification of scarlet fever toxoid can easily be determined. The toxicity of scarlet fever toxoid determined by trial with white pigs generally agrees with that determined by the rabbit ear skin method.

AUTHOR'S SUMMARY.

Chronic Infections

CHILDHOOD-TYPE TUBERCULOSIS AS REVEALED BY THE X-RAY. H. F. R. WATTS, Am. Rev. Tuberc. **29**:424 (April) 1934.

In many cases the childhood type of tuberculosis is incapable of roentgenographic demonstration, partly because present roentgen technic is not sufficiently delicate and partly because such structures as uncalcified tracheobronchial, mediastinal and hilar lymph nodes are not shown unless they are of extraordinary size. The shadow of the normal hilus is largely that of its blood vessels and of the reflected pleura. The bronchi beyond the main bronchus cannot be differentiated except when caught end-on, this giving the image a cross-section. The so-called "thickened hilus shadow" may be due to undifferentiated, soft enlargement of lymph nodes within the structure of the hilus or to engorgement or motion, or both, of its blood vessels from cardiac systole at the moment of exposure. Shadows of axial vessels may be mistaken for calcified lymph nodes, but are readily differentiated in stereoscopic films. In most instances the lesions in the childhood type of tuberculosis may be demonstrated only after they have begun to calcify. The calcium shadow is usually granular and of definitely greater density than its surroundings. The presence of such calcified areas, whether within the lymph nodes or in the parenchyma of the lung, is accepted as evidence of the childhood type of tuberculosis. Obviously this change occurs comparatively late in the tuberculous cycle. A study of successive x-ray films has led Watts to classify as "childhood-type in the making" pneumonic shadows which are slow to resolve, leaving progressively sharper shadows of striated fibrosis and, finally, calcium shadows in adjacent hilar areas and perhaps at the site of the original pneumonia.

EUGENE SMITH, Ogden, Utah.

TUBERCULOSIS IN NEGRO CHILDREN. COLE B. GIBSON, Am. Rev. Tuberc. **29**:430 (April) 1934.

For the past seven years, twelve persons in every five hundred of the population of Connecticut have been Negroes. During the same period, among every five hundred patients admitted to the children's sanatorium forty-one were colored children. In every group of twenty-five white children admitted one died; whereas in every group of twenty-five colored children admitted four succumbed. This study fails to throw any light on the reasons for these differences between tuberculosis in Negroes and white persons. A distinct impression is left, however, that the Negro child reacts violently to first infection, contracts serious tuberculous disease at an earlier age, is subject to more frequent associated lesions and complications and surrenders earlier to lethal disease than the more immunized white child. It appears that whereas first infection with tubercle bacilli modifies the resistance of the white child to future infections, similar immunologic reactions do not occur in the colored child, even though a state of allergy may develop, so far as a positive response to tuberculin is concerned.

EUGENE SMITH, Ogden, Utah.

TUBERCLE BACILLI IN THE GASTRIC CONTENTS OF TUBERCULOUS CHILDREN. INA GOURLEY, Am. Rev. Tuberc. **29**:461 (April) 1934.

Fifty-nine cases of the childhood type of tuberculosis were studied by gastric lavage and by inoculation of guinea-pigs. In twenty-eight of these, or 47.4 per cent, tubercle bacilli were found in the gastric contents. In 56 per cent of the fifty children with demonstrable lesions cultures of the gastric contents were positive. This study apparently indicates that all types of parenchymal lesions in the childhood type of tuberculosis, including the "C" group of McPhedran's classification, are open cases.

EUGENE SMITH, Ogden, Utah.

THE DEMONSTRATION OF TUBERCLE BACILLI IN THE SPUTUM, FAECES AND STOMACH CONTENTS OF TUBERCULOUS CHILDREN. LUCY MISHULOW, CAMILLE KERESZTURI and DAVID HAUPTMAN, Am. Rev. Tuberc. **29**:471 (April) 1934.

A comparative study was made of the feces, contents of the stomach and, in some cases, the sputum of sixty tuberculous children. Smears of the feces were positive for tuberculosis in twelve patients, and smears of the gastric contents were positive in sixteen. Smears of both feces and the gastric contents were positive in eleven of these; a smear of the feces only was positive in one, and smears of the gastric contents only, in five. Of forty-four specimens of gastric contents that were negative in all examinations of smears, four were positive on the inoculation of guinea-pigs. The feces were not examined by the inoculation of guinea-pigs. The results of examination of the sputum corresponded closely to those of examination of the gastric contents. The inoculation of guinea-pigs should be done as a final confirmation when specimens are negative on examination of smears, and repeated examinations should be made in doubtful cases. The indications are that repeated examinations of the feces by smear and inoculation may prove as satisfactory as the examination of specimens obtained by gastric lavage. In the sixty cases in this series, examination of the feces, gastric contents and sputum (when obtained), gave positive results in 10 per cent of the children who were apparently well at the time of examination, in 54.5 per cent of those who were slightly ill and in 63.1 per cent of those who were very ill. Of the children who had destructive parenchymatous pulmonary tuberculosis, 83.3 per cent showed positive results, and of those who had nondestructive parenchymatous lesions, 24 per cent showed positive results. In all the patients who had only positive intracutaneous reactions tuberculosis of the hilar lymph nodes, pleurisy with effusion and tuberculous peritonitis the results were negative.

EUGENE SMITH, Ogden, Utah.

TUBERCLE BACILLI IN THE SPUTUM AND FAECES OF CHILDREN WITHOUT PULMONARY TUBERCULOSIS. J. P. NALBANT, Am. Rev. Tuberc. **29**:481 (April) 1934.

Tubercle bacilli were demonstrated in the contents of the gastro-intestinal tract in seven of nineteen children who had no demonstrable pulmonary tuberculosis. Of the several possible sources of the bacilli, the most probable are a receding type of parenchymal infiltration which has cleared roentgenologically yet is not completely rid of the bacilli, and the breaking down of a tuberculous tracheobronchial lymph node and the emptying of its contents into a bronchus for eventual swallowing. A child with tubercle bacilli in the stools or the contents of the stomach is a menace to others and should be isolated and treated as tuberculous even though the source of the bacilli may not be evident.

EUGENE SMITH, Ogden, Utah.

THE RELATION OF ALLERGY TO IMMUNITY IN TUBERCULOSIS. HERBERT ROTHSCHILD, JONAS S. FRIEDENWALD and CLARENCE BERNSTEIN, Bull. Johns Hopkins Hosp. **54**:232 (April) 1934.

This paper is too long to be summarized satisfactorily and should be read by those interested in the nature of immunity and the question as to whether immunity is dependent on the existence of allergy. The authors' conclusions follow:

Complete desensitization to tubercle bacilli and to tuberculin can be achieved in tuberculous guinea-pigs by a prolonged and properly graded course of subcutaneous injections of Koch's old tuberculin. The desensitizing power of purified tuberculoprotein is less in proportion to its power to produce allergic reactions than is that of Koch's old tuberculin.

Long continued daily subcutaneous injections of massive doses of concentrated glycerin broth in some instances desensitize tuberculous guinea-pigs to tuberculin. This nonspecific desensitization is not due to the glycerin contained in the broth. It is not known whether such desensitization is free from the danger of perifocal reaction.

Infection in desensitized immune animals does not introduce into the histologic picture of tuberculous lesions features that are novel to the pathologic changes in human tuberculosis.

In all these respects the reactions of the desensitized animals were equal or superior to those of the nondesensitized controls. So far as the inhibition of spread of lesions from the site of infection to the viscera may be used as evidence of local fixation of bacilli, the desensitized, nonallergic immunes were able to resist the spread of infection as successfully as the allergic immunes.

LYTTLE, New York.

THE CLINICAL BASIS AND PRESENT STATUS OF VACCINATION AGAINST TUBERCULOSIS. CLEMENT A. SMITH, New England J. Med. **211**:147 (July 26) 1934.

In the studies made by Park and his associates in New York, and by Wallgren in Gothenburg on tuberculous contacts the results were practically the same; i. e., there was no mortality from tuberculosis in the inoculated subjects, as against about 3 per cent mortality in the controls, both studies indicating the safety of the methods used.

Smith first discusses the results obtained with the various methods of producing immunization against tuberculous infection in experimental laboratory animals. Guinea-pigs and rabbits immunized with B C G or killed bacilli lived twice as long after a subsequent virulent infection as the control animals. Those immunized with killed bacilli lived longer than those immunized with living attenuated bacilli. The best results were obtained when the intracutaneous method of immunization was used.

GENGENBACH, Denver.

SYMPTOMS AS A MEASUREMENT OF TUBERCULOUS ACTIVITY. HARVEY S. WAGNER, New England J. Med. **211**:237 (Aug. 9) 1934.

The constitutional symptoms of tuberculosis include fever, a rapid pulse rate, weakness, emaciation, loss of appetite and sweating. Of these, weakness, sweating and loss of appetite and weight generally appear the first to be overcome as improvement occurs. Inability to gain weight within a month, also loss of from 30 to 40 per cent of the normal weight, is serious. Intermittent fever, with the temperature varying from subnormal in the morning to 102 F. at night, becomes of grave significance after continuing two months. It is due not only to the absorption of toxins of the bacillus, but also to the absorption of broken-down tissue products of tubercles in advanced stages of the disease. Chills, sweating and great loss of weight and strength are associated with fever of this sort.

A pulse rate of more than 85 in the male and more than 90 in the female should suggest activity, in making a diagnosis, or reactivity in cases in which the disease was apparently arrested. Cough alone cannot be depended on to indicate a diagnosis, because too many other conditions produce it, but the appearance of secretion with tubercle bacilli indicates potential trouble. When hemoptysis occurs, it means advancing disease from the practical standpoint of treatment by rest.

GENGENBACH, Denver.

THE MONOCYTE-LYMPHOCYTE RATIO AS A MEASUREMENT OF ACTIVITY IN PULMONARY TUBERCULOSIS. GULLI LINDH MULLER, New England J. Med. **211:** 248 (Aug. 9) 1934.

All the blood counts were made by one person on fixed cover slip smears, according to standard procedures. Among 800 patients admitted consecutively to the Rutland State Sanatorium, 730 had pulmonary tuberculosis; 13, the childhood type of tuberculosis, as a rule, inactive; 7, pleurisy with effusion, and 50, nontuberculous disease. The majority of the patients with the childhood type of tuberculosis and with conditions classified as nontuberculous had a practically normal monocyte-lymphocyte ratio.

The prognosis represented the consensus of the majority of the staff of the sanitorium. The number of patients for whom a favorable prognosis was given decreased as the monocyte-lymphocyte ratio increased, and vice versa.

Among the group of 111 patients with a normal monocyte-lymphocyte ratio 88.2 per cent improved. As the percentage of those who improved decreased the monocyte-lymphocyte ratio increased. This ratio also increased proportionally to the increasing number of patients who showed no improvement or who died.

A high ratio may be accounted for by various factors, such as an acute onset with a cold, bronchopneumonia, pneumonia or pleurisy. Successful active therapy may also bring about a rapid change in the monocyte-lymphocyte ratio. However, 25 per cent of the patients with a ratio of more than 1 died within three months. Many of the patients with a normal ratio showed an increase in the sedimentation rate and a shift to the left in the polymorphonuclear differential count. The monocyte-lymphocyte ratio, therefore, is not a sensitive index of activity in the tuberculous patient. However it is a delicate, easy measure of the resistance of the host to the invader.

GENGENBACH, Denver.

THE PREVENTION AND CONTROL OF TUBERCULOSIS IN THE COMMONWEALTH OF MASSACHUSETTS. FREDERICK T. LORD, New England J. Med. **211:**312 (Aug. 16) 1934.

The Massachusetts Tuberculosis League and its affiliated organizations play an important part in formulating public opinion in favor of the investigation of tuberculous contacts and the breaking of contacts and in cooperation with physicians and boards of health in making the investigation possible. Sources of information with respect to undiscovered cases of tuberculosis are reports of cases, reports of deaths and the results of the investigation of school and camp children.

Restriction of the advantages of the summer health camps for the most part to those with the milder forms of the childhood type of tuberculosis, persons with suspicious cases, contacts reacting to tuberculin and reactors with malnutrition offers the opportunity of preventing further infection in the individual and of controlling the disease in the community.

A period of less than two months in the camp may be regarded as undesirable. All candidates for the camps should be given the Schick test, and the reactors should be immunized against diphtheria.

GENGENBACH, Denver.

A CASE OF TUBERCULOUS MENINGITIS WITHOUT CELLULAR REACTION. MIHAIL CAMNER and MARIE CAMNER, Bull. Soc. de pédiat. de Iasi **5:**27 (Jan.-March) 1934.

A 4½ year old boy with pulmonary and hilar tuberculosis had headache, fever, convulsions, facial paralysis, strabismus and rigidity of the neck. Lumbar puncture revealed clear fluid, with a positive Pandy reaction and only 4 lymphocytes to the cubic millimeter. A pellicle of fibrin formed in the fluid; smears from this revealed tubercle bacilli. This case was undoubtedly one of tuberculous meningitis without an increased cell count in the spinal fluid. No definite reason for the absence of pleocytosis could be ascertained, although several possibilities are discussed.

LEMASTER, Evanston, Ill.

ORGANIZATION OF THE FIGHT AGAINST TUBERCULOSIS AND SYPHILIS IN CHILD WELFARE WORK. MANUEL MIRALBELL, But. Soc. catalana de pediat. **4**:194, 1931.

The prevention of tuberculosis consists in the prevention of contagion, the immunization of the infant and the improvement of the general hygiene. Mortality was reduced in the first year by means of vaccination with B C G from 19.6 per cent in the unprotected group studied to 5 per cent in the vaccinated group. Premarital examinations are desirable in preventing syphilis. The organization of local units for education and clinical treatment is advocated.

WATSON, Elmhurst, Ill.

SILICA AND TUBERCULOSIS. DECREF, Med. de los niños **35**:140 (May) 1934.

A study was made to determine the relation of silicic acid in the body to tuberculosis. Determinations were made of the silicic content of the various bovine organs and compared with the findings in the human lung. The highest concentration was found in the pancreas, the one organ that is rarely infected by tubercle bacilli. The distribution of silicic acid in the human lung showed the least amounts in the upper lobe of the right lung, larger amounts in the upper lobe of the left lung, still larger amounts in the middle lobe of the right lung and the lower lobe of the left lung and the largest amounts in the lower lobe of the right lung, which corresponds to the topographic distribution of tuberculosis in the various lobes.

DWYER, Kansas City, Mo.

A CASE OF FOLLICULAR HEPATIC HYPERTROPHIC TUBERCULOSIS WITH PERIPORTAL ADIPOSE INFILTRATION. M. ECHEGARAY, But. Soc. catalana de pediat. **5**:7, 1932.

A case is reported of a child 10 years of age who had had fever for seven months. The liver and spleen were greatly enlarged, and a right pleural effusion was present. The Mantoux reaction was strongly positive. A portion of the liver removed for section revealed the typical structure of tuberculosis. The periportal extensions were converted into fat cells. The child died of tuberculous meningitis.

WATSON, Elmhurst, Ill.

THE DE COSTA REACTION IN TUBERCULOUS INFANTS. GUSTAVO GARCIA ALVAREZ, Rev. chilena de pediat. **5**:140 (March) 1934.

The de Costa reaction is a nonspecific precipitive reaction of tuberculosis. Only reactions which appear before ten minutes after its use must be considered, as reactions occur in normal persons after ten minutes. The reaction runs parallel to the sedimentation reaction; at times it is more sensitive than the latter. Both are based on the same fundamental process (alteration in the composition of the blood proteins). Like the sedimentation test, it can serve as a means by which one can follow the results of treatment. In tuberculosis the intensity of the reaction parallels the activity of the process.

Since it is a very sensitive reaction it must be frequently repeated. It is of great value in detecting early primary infection, as it is positive much earlier than any tuberculin reaction. In early tuberculosis the de Costa reaction is much more sensitive than the sedimentation reaction. In chronic or surgical tuberculosis the reverse is the case.

SCHLUTZ, Chicago.

THE EOSINOPHIL EPINEPHRINE REACTION IN TUBERCULOSIS. TIBOR VON KROMPASZKY, Monatschr. f. Kinderh. **60**:321, 1934.

In a well child the blood reaction following the injection of epinephrine consists in an increase in the eosinophil count. The reaction occurs within from one-half hour to one and one-half hours and is over in two and one-half hours. Frequently the leukocytes are also increased.

In a study of twenty-eight cases of tuberculosis Krompaszky found the reaction normal in one half, while in the other half the eosinophil count diminished following the injection. The normal reaction occurred in the mild cases, the abnormal in the severe cases.

Krompaszky does not believe that the reaction is specific but thinks that it is simply a reaction caused by epinephrine, in which the eosinophils are squeezed out in the normal bone marrow and there is no effect on the diminished number of eosinophils in the depleted bone marrow in the severer cases.

GERSTLEY, Chicago.

Internal Diseases

MORTALITY IN DIABETIC CHILDREN. HENRY J. JOHN, Am. J. Digest. Dis. **1**:180 (May) 1934.

This is an interesting article, including reports of cases of patients treated in the pre-insulin era. The early and proper use of insulin is the factor by which the death rate has been lowered. Two hundred and fourteen cases are reported, with twenty-eight deaths (13 per cent mortality). Sixty-four per cent of the deaths resulted from coma. Deaths from tuberculosis were 10.6 per cent.

MORRISON, Savannah, Ga.

X-RAY'S CONTRIBUTION TO THE DIAGNOSIS OF THE "ACUTE ABDOMEN." WILLIAM H. STEWART and H. EARL ILLICK, Am. J. Digest. Dis. **1**:185 (May) 1934.

The authors list the following conditions in which the roentgen rays help in the diagnosis: (1) obstruction; (2) perforation; (3) rupture of the kidney; (4) acute inflammation, appendicitis or cholecystitis; (5) intussusception; (6) colic, either biliary or urinary, and (7) hemorrhage from an ulcer or a malignant growth. The roentgen findings are, of course, always in conjunction with the history and the physical findings.

MORRISON, Savannah, Ga.

NEUROBLASTOMA METASTASES IN BONES, WITH A CRITICISM OF EWING'S ENDOTHELIOMA. R. A. COLVILLE and R. S. WILLIS, Am. J. Path. **9**:421 (July) 1933.

A suprarenal neuroblastoma in an 8 year old girl caused metastases in the bone which were morphologically identical with Ewing's sarcoma. It is suggested that Ewing's sarcoma is a metastatic tumor of bone and is not primary.

MOORE, New York.

RHEUMATIC HEART DISEASE WITHOUT VALVULITIS. C. Z. GARBER, Am. J. Path. **9**:443 (July) 1933.

A case of chronic rheumatic disease without disease of the valves in an 8 year old Chinese girl is reported. Aschoff bodies were not found. The diagnosis of rheumatic fever was based on characteristic lesions in the left auricle and vascular system and diffuse infiltration of the heart. Seventeen similar cases in the literature are reviewed.

MOORE, New York.

"THE COMMON COLD." DAVID THOMSON and ROBERT THOMSON, Ann. Pickett-Thomson Research Lab. **8**:1 (Dec.) 1932.

This volume, consisting of 738 pages, contains information extracted from more than 2,000 articles, together with a short account of the authors' researches on the subject of the common cold.

Every major item of the subject is covered—the structure and physiology of the nose, the anatomy of the sinuses, normal bacterial flora, the chemistry of the mouth and saliva, the various claimed causes of colds and the rôles of various micro-organisms. This is a book that is as important to the average practitioner as to the research worker. The effect of chills, bad ventilation, fatigue, diet and clothing are considered in detail and make the volume valuable to every one in the medical field. The complications and sequelae of colds are adequately dealt with, as are the methods of protection, such as vaccines and sprays. There is more information on the common cold packed in this volume than has ever before been collected in one book.

A glance at the publication is sufficient to make one wish to own a copy.

TOOMEY, Cleveland.

MECKEL'S DIVERTICULUM. R. N. SCHULLINGER and A. P. STOUT, Arch. Surg. **28**:440 (March) 1934.

A unique case of Meckel's diverticulum is reported in which the mucosal surface near the tip was the site of a nonulcerated pedunculated adenoma composed of gastric and duodenal glands. The symptoms noted emphasized the fact that severe acute symptoms, including abdominal pain and bleeding from the rectum unmixed with mucus, may occur in persons with Meckel's diverticulum without any evidence of invagination, intussusception or ulceration. A thorough review of the literature was made to determine the symptoms associated with this condition. The authors conclude that search for a Meckel's diverticulum should always be made when there is unexplained bleeding by rectum or peritonitis of undetermined origin or when the operative findings are not in accord with the clinical diagnosis.

KAISER, Rochester, N. Y.

CONSTITUTION AND ALLERGIC MANIFESTATIONS: I. AGE-SEX INCIDENCE OF ALLERGIC CONDITIONS. TELL NELSON, J. Allergy **5**:124 (Jan.) 1934.

The age-sex incidence of asthma, hay fever or allergic dermatosis was studied in 1,786 persons. These conditions predominate in males in the proportion of 2:1 in the first decade. In females they predominate in the proportion of 5:3 in the second decade. The distribution is fairly equal from the middle of the second decade on.

Hay fever occurred in 856, asthma in 743 and allergic dermatosis in 187 of the 1,786 persons studied. Of the persons with hay fever and asthma, 55 per cent were males and 45 per cent females; of the group of those with dermatosis, 37 per cent were males and 63 per cent females.

The incidence in the first decade shows the percentage of the total for the decade in both sexes to be parallel in each of the three groups.

There is an equally high incidence of allergic dermatosis in the first year of life and a marked drop in the second year in both sexes. HOYER, Cincinnati.

THE THYMUS GLAND AND THYMIC SYMPTOMS. AARON CAPPER and ROBERT A. SCHLESS, J. Pediat. **4**:573 (May) 1934.

More than 1,000 new-born infants were examined for evidence of thymic enlargement. The roentgenologic reports indicated thymic enlargement in 30 per cent, but after careful analysis thymic symptoms due to thymic enlargement could be ascribed with certainty to only 0.56 per cent.

The authors believe that the diagnosis of an enlarged thymic gland is made too frequently. It is considered inadvisable, unnecessary and economically inexpedient to make a routine examination of every new-born infant with the roentgen rays for evidence of thymic enlargement. Roentgen treatment directed to the thymus should be carried out only when other causes of the symptoms have been carefully ruled out and when the roentgenologist has demonstrated unmistakable evidence of enlargement.

LEMASTER, Evanston, Ill.

DIATHERMY IN THE TREATMENT OF PNEUMONIA. HARRY E. STEWART, Brit. J. Phys. Med. **8**:133 (Jan.) 1934.

The author describes his apparatus and technic for the use of diathermy in the treatment of pneumonia. Among the symptomatic effects of such treatment he noted a decrease in cyanosis, a tendency for the tenacity of the mucus to be lessened and a lowering of the temperature. He reports that in 97 per cent of his patients with lobar pneumonia the drop in temperature was by lysis. In his series of about 1,000 cases the mortality rate was 11.9 per cent.

HARTMAN, Cleveland.

BRONCHIECTASIS. W. L. ROBINSON, Brit. J. Surg. **21**:302 (Oct.) 1933.

The pathology and histopathology in sixteen cases in which lobectomy was performed are presented. Robinson found that the most consistent pathologic change was a chronic inflammatory condition of the bronchial walls, with various degrees of damage up to complete destruction of the musculo-elastic tissue. He states that infection of the wall seems to be of prime importance in the development of the diseases. In the early stages the condition is probably of the nature of paralysis of the muscular system, leading to loss of tone with consequent dilatation. Provided the infection is of short duration, recovery may occur. When infection persists for a longer period permanent damage occurs; the elasticity of the wall is lost, and its dilations become fixed. Mechanical obstruction, such as an aspirated foreign body or a tumor, is found in certain cases, but no obstruction was found in this series. The vascular changes which occur in the bronchial arteries are important, as they lower the resistance of the tissues and favor the persistence of the infection.

SUMMERFELDT, Toronto, Canada.

THE DEFICIENCY ANAEMIAS OF CHILDHOOD. LEONARD G. PARSONS, Brit. M. J. **2**:631 (Oct. 7) 1933.

Parsons defines deficiency anemia as an anemia which is due to an insufficient supply of one or more of the elements necessary for the synthesis of hemoglobin, for the production of erythrocytes or for both; such deficiency may be the result of an inadequate diet, defective absorption from the alimentary canal or failure of the body to elaborate certain substances which are essential for normal erythropoiesis.

He then discusses briefly the recent history of the study of the primary and the secondary and deficiency types of anemia. Then follows an interesting résumé of hemopoiesis, with mention of all the underlying factors and differentiation of the blood cells according to their age and form. He stresses two types of deficiency anemia, the hyperchromic and the hypochromic. Because the hypochromic type is rarely fatal, little work has been done on the bone marrow in anemia.

The author then discusses his own studies in a case of hypochromic anemia associated with celiac disease and mentions three outstanding features: (1) the replacement of a considerable part of the marrow by a structureless, red, jelly-like material; (2) the presence of foci of erythropoiesis in which there was a fair proportion of young nucleated red cells, the majority being of the normoblastic type, megaloblasts being absent, and (3) slight immaturity of the myeloid cell series. These are interpreted as normoblastic reaction of the marrow in which hyperplasia was giving way to hypoplasia. The maturation of the normoblast into an erythrocyte and the prevention of the normoblastic reaction in bone marrow are brought about only by an adequate supply of iron, copper, vitamin C and thyroxine.

Hyperchromic deficiency anemia occurs in children in rare conditions, such as celiac disease. Hypochromic deficiency anemias include common nutritional or alimentary anemias of infancy, some of the anemias associated with celiac disease, the anemia occurring in scurvy and that occurring in cretinism.

A brief summary follows, explaining the changes in the blood of normal and anemic children in the first year of life. "Nutritional or alimentary anemia in infants" as a specific term applies to the forms of deficiency anemia which are due to an inadequate supply of iron (or iron and copper). The prevalence of this form is widespread, and the patients are usually subject to other illnesses, such as infections, although they are well grown and well nourished in many instances, being merely pale. The spleen, although frequently enlarged, is not of great importance. The lymph glands are not enlarged. There are frequently achlorhydria and changes in the color of the skin. The most frequent deficiency in this group of anemias is iron deficiency; sometimes copper deficiency may play a part, and likewise the factors contained in yeast may be lacking. The mechanism of the development of the defects of this type of anemia is discussed under three headings: (1) deficient antenatal storage, (2) deficient postnatal supply and (3) deficient antenatal storage and postnatal supply. Iron alone effects a cure in some instances, while in others copper is necessary. The best single agent is iron and ammonium citrate, which is probably slowly broken down in the stomach, with the formation of ferrous salts. It is likely that copper is not necessary for the assimilation of iron, but it is necessary for the synthesis of hemoglobin. Copper, therefore, apparently affects only the hemoglobin, not influencing reticulocytosis. Yeast is sometimes a valuable adjunct, but its mode of action is not clear.

Either type of anemia may occur in celiac disease. The hypochromic form is much more common, and a cure may be obtained by adequate doses of iron. The anemia incident to scurvy is discussed, and points of view in regard to this condition are brought out. Vitamin C alone probably cures this, but in any event copper should not be added to the diet, because it destroys vitamin C. The anemia of cretinism is probably due to a deficiency in thyroxine.

Hyperchromic deficiency anemias are discussed rather briefly, owing to their rarity and the doubt of the accuracy of the diagnosis. It is still doubtful whether true Addison's anemia has ever been seen in infants or young children. This form of anemia has been described by a number of observers and is regarded as due not to absence of the intrinsic factor, as in the case of pernicious anemia, but to absence of the extrinsic factor, and it is thought that the latter can be supplied and the anemia cured by the administration of autolyzed yeast (B_2). Brief mention is also made of bothriocephalus anemia.

ROYSTER, University, Va.

"BORNHOLM" DISEASE. W. N. PICKLES, Brit. M. J. **2**:817 (Nov. 4) 1933.

This is an account of an outbreak of this disease in one family, with a possible source from a visitor. The name used by the author is derived from the island of Bornholm in the Baltic Sea. The disease was first described in the United States in 1888 by Dabney and is called by various names, such as "myositis acuta epidemica," "devil's grip" and "epidemic transient diaphragmatic spasm."

ROYSTER, University, Va.

A CASE OF VON GIERKE'S "GLYCOGEN ACCUMULATION DISEASE." H. J. SOLOMON and P. M. ANDERSON, M. J. Australia **2**:660 (Nov. 11) 1933.

The authors report a case of von Gierke's "glycogen accumulation disease" in a 2 year old child. The manifestations consisted of hepatomegaly, ketonuria, hypoglycemia, lipemia (which later disappeared) and mild epileptiform seizures. The latter attacks ceased on the administration of an abundance of dextrose. The child was alive and well at the time of writing. Only four previous cases have been reported. Theories as to the cause of the symptoms are summarized as follows: 1. The retention of glycogen due to the absence of the normal glycogen-splitting ferment in the liver leads to enlargement of this organ. 2. Glycogen being retained, sugar is not available for the complete combustion of fats, and ketonuria results. 3. A portion of the glycogen of the liver is converted into fat, thereby producing lipemia. 4. The diminished absorption of fat due to the diminished flow of bile

(caused by pressure of the glycogen-distended cells of the liver on the biliary capillaries) leads to steatorrhea. 5. Hypoglycemia and ketonuria produce epileptiform seizures.

GONCE, Madison, Wis.

HOUSING CONDITIONS AND RESPIRATORY DISEASE. C. M. SMITH, Medical Research Council, Spec. Rep. Ser., 1934, No. 192.

This study deals with an inquiry into the amount, nature and incidence of illness occurring during one year among a population of nearly 2,000 in a poor district of Glasgow. Acute respiratory disorders accounted for almost half the total morbidity. Tuberculosis, acute infectious diseases and chronic respiratory disorders came next in importance. The number of fatal cases of pneumonia was high, but this was ascribed to a higher incidence of pneumonia in districts in which the poor class lived rather than to an excessive fatality. An epidemic of influenza occurring during the period of study provided an opportunity for observing the age at incidence, the clinical type and the mode of spread of this disease.

Half the population under study was housed in a district of the slum type, and the other half in a rehoused area. Comparison of the morbidity in the two groups did not yield conclusive results. Although the persons in the rehoused area had more rooms per person than those in the slum district, they often retained the slum habit of crowding into one room at night, especially in winter.

LEMASTER, Evanston, Ill.

ANEMIA: PROBABLY ACHOLURIC JAUNDICE. E. C. WARNER, Proc. Roy. Soc. Med. **26**:1374 (Aug.) 1933.

This article reports the case of a girl of 5 years. The spleen was 1½ inches (3.77 cm.) below the umbilicus; the liver was slightly enlarged. and the skin at times became lemon-yellow. The blood count showed: red cells, 3,400,000; hemoglobin, 38 per cent, and white cells, 6,800. The result of the van den Bergh test (indirect) was 2 units. A fragility test showed that hemolysis was complete in from 0.4 to 0.3 per cent of sodium chloride. In spite of treatment with liver and iron for six months the child showed no improvement

WILLIAMSON, New Orleans.

ATELECTATIC BRONCHIECTASIS. DONALD PATERSON, Proc. Roy. Soc. Med. **27**:121 (Dec.) 1933.

A patient, aged 4½ years, had a history of pneumonia at the age of 1 and 3 years and twice during the year before admission to the hospital, with a third attack in the same year. Physical examination revealed an impaired note on percussion, bronchial breathing and a few rhonchi at the base of the left lung posteriorly. Roentgenograms first showed complete collapse of the lower lobe of the left lung. Two months later, a roentgenogram suggested collapse and bronchiectasis of the base of the left lung. The injection of iodized poppy-seed oil showed 40 per cent collapse of the lower lobe of the left lung—not an accessory lobe, also bronchiectasis in the atelectatic area.

WILLIAMSON, New Orleans.

TRAUMATIC PNEUMOTHORAX WITH DISPLACEMENT OF THE MEDIASTINUM TOWARDS THE SIDE OF THE PNEUMOTHORAX. WILFRID SHELDON, Proc. Roy. Soc. Med. **27**:125 (Dec.) 1933.

A girl, aged 6 years, was knocked down by a lorry. When seen about one hour after the accident she had considerable surgical emphysema of the neck and over the front of the chest. A roentgenogram showed fracture of the third rib on the right side and right-sided pneumothorax. The surgical emphysema cleared up within a week, but the patient was left with complete right-sided pneumothorax,

the right lung being fully collapsed. The air in the pneumothorax slowly absorbed, but instead of the lung expanding there was a steadily increasing shift of the heart and mediastinal structures to the right side.

WILLIAMSON, New Orleans.

INTESTINAL HEMORRHAGES AND DYSCRASIA OF THE BLOOD IN A BOY NINE AND A HALF YEARS OLD. P. NOBÉCOURT, R. LIÈGE and GRODNITSKY, Bull. Soc. de pédiat. de Paris **31**:324 (July 11) 1933.

A well developed and well nourished boy, 7 years and 2 months old, had repeated melena and was very pale. Physical examination as well as a series of roentgenograms of the gastro-intestinal system following the ingestion of barium sulphate showed nothing abnormal. Hematologic investigation revealed severe anemia, delayed coagulation of the blood, poor retraction of the blood clot and thrombocytopenia. After several months the intestinal bleeding ceased, and examination of the blood showed progressive improvement of the anemia, with disappearance of the abnormalities. Exploratory laparotomy had been suggested on the assumption that the bleeding might have occurred from an ulcer of a Meckel's diverticulum, but postponement of the operation was decided on in view of the abnormal blood findings. It is believed that the intestinal hemorrhages were due to a temporary disturbance of the blood.

BENJAMIN, Montreal, Canada.

DIAGNOSIS OF CONGENITAL CYST OF THE LUNG IN A RECENT CASE. R. DEBRÉ, M. MIGNON and ODIER-DOLLFUS, Bull. Soc. de pédiat. de Paris **31**:329 (July 11) 1933.

A girl, 5 months old, was admitted to the hospital because of an infection of the upper respiratory tract and diarrhea. She had a loud systolic murmur due to an interventricular septal defect. Roentgenologic examination of the chest confirmed the presence of a congenital cardiac abnormality of the type seen in Roger's disease. A shadow on the right side of the chest in the form of a bar extending from the heart to the outer wall of the chest at the level of the junction of the upper third and the lower two thirds was noted. No physical findings were made out which would lead one to suspect any pulmonary lesion. Two months later another roentgenogram of the chest showed an increase of 5 mm. in the width of the right side of the chest as compared with the width of the left side. The shadow on the right side had increased and had moved upward, involving the entire upper lobe, which seemed to be compressed, with the lower border now concave on its inferior aspect; below this the lung appeared hyperventilated but with bronchovascular markings running through it, and there was an increase in the size of the cardiodiaphragmatic angle so that the clear area encroached on the lower part of the right border of the heart. On physical examination a tympanitic note and diminished breath sounds over the lower half of the posterior part of the right side of the chest were present. The infant had acute bronchitis, with some dyspnea, but no cyanosis on several occasions in the interval, and had gained weight regularly. The condition was diagnosed as a congenital air cyst of the lung. No report of the subsequent course is given.

BENJAMIN, Montreal, Canada.

AIR CYST OF THE LUNG. R. DEBRÉ and E. GILBRIN, Bull. Soc. de pédiat. de Paris **31**:332 (July 11) 1933.

Following a previous communication concerning a congenital air cyst of the lung in an infant, Debré and Gilbrin report a similar condition in a man 33 years old. The provisional diagnosis was spontaneous pneumothorax, which was permissible from the signs and symptoms. However, careful examination of a roentgenogram of the chest showed that a congenital air cyst was present in the lower part of the right lung. Exploratory puncture as well as roentgen examina-

tion following the injection of iodized poppy-seed oil 40 per cent are contraindicated in this condition. The acute onset of symptoms in patients with this abnormality, which usually occurs at an early age and is therefore of particular interest to pediatricians, is due to the opening of a cyst into a large bronchus or the fusion of multiple cysts into one large pocket of air.

BENJAMIN, Montreal, Canada.

PNEUMONIC PROCESS INVADING SUCCESSIVELY THE THREE LOBES OF THE RIGHT LUNG. B. WEILL-HALLÉ and A. ABAZA, Bull. Soc. de pédiat. de Paris **31**:334 (July 11) 1933.

A boy, 3 years old, showed involvement of the base of the right lung, followed by consolidation of the middle lobe about the eighth day of the acute illness; this was followed several days later by consolidation of the apex of the right lung. Roentgenograms of the chest, taken on the three occasions when the clinical signs pointed successively to involvement of the lower, middle and upper lobes, confirmed the physical findings. Several weeks later the child was discharged from the hospital cured.

BENJAMIN, Montreal, Canada.

SPLENOMEGALIC ANEMIA AND MENINGEAL HEMORRHAGE. B. WEILL-HALLÉ and A. ABAZA, Bull. Soc. de pédiat. de Paris **31**:340 (July 11) 1933.

A boy who had been born prematurely showed severe anemia of the hypochromic type at 1 year of age. The spleen was enlarged. He had shown evidence of frequent digestive disturbances since birth and had been fed nothing but milk. All these factors contributed to the production of a high degree of anemia of a common type. The interest in the case centered around an unusual complication, viz., meningeal hemorrhage, with signs of meningeal irritation and bloody spinal fluid obtained by lumbar as well as cisternal puncture. This cleared up within a few days, but the anemia showed little improvement after he was given a diet high in iron, an inorganic iron preparation and a preparation of liver. He was also given mercurial inunctions, although all tests for syphilis gave negative results. After two small blood transfusions the anemia began to improve markedly.

BENJAMIN, Montreal, Canada.

ACUTE MONOCYTIC LEUKEMIA. G. ANDREOLI and E. FOUREST, Bull. Soc. de pédiat. de Paris **31**:351 (July 11) 1933.

A boy, 8 years old, who had been well up to about six weeks previously, had become very pale and weak. He had lost weight and had begun to have fever, which became more and more marked. He had a reddened throat, multiple adenopathies and splenomegaly, and a number of small cutaneous hemorrhages developed. Hematologic studies revealed a high leukocytosis, with a very high percentage of monocytes, some diminution in the number of lymphocytes and practically no granulocytes. The red blood cell count was low; the hemoglobin was low, and there were many immature red cells, moderate poikilocytosis and anisocytosis. The blood platelets were low; the tourniquet test gave positive results; the coagulation time of the blood was within normal limits; the blood clot showed no retraction; the bleeding time was increased, and the sedimentation time was very high. The child's condition became steadily worse, and he died fifteen days after he was first examined. Infectious mononucleosis is ruled out because of the severe anemia, hemorrhages and disturbances in the bleeding and clotting of the blood and the rapidly fatal issue. Agranulocytosis is ruled out because of the absence of leukopenia, the high monocyte count, the presence of cutaneous hemorrhages and the abnormal blood findings. The diagnosis arrived at is acute leukemia of the monocytic type, which has been described by several observers within recent years.

BENJAMIN, Montreal, Canada.

ACUTE LEUKEMIA IN A LITTLE GIRL. CAMILLO CISI, Pathologica **25**:474 (July 15) 1933.

Cisi reports a case of acute leukemia characterized by the presence of many monocytic and lymphocytic cells, fewer myeloid and histioid cells, many so-called monocytoid cells and other leukocytic elements. There were numerous Auer's bodies (their relations with the nuclei would confirm their nuclear origin) and particular forms with karyokinesis.

The author summarizes the question of the origin of the monocytes, and appears to be in favor of a unitarian-tricomposed theory, which explains the morphogenesis of the different types of monocytic leukemia; he believes that this theory (together with the aforementioned leukemia esteemed as a nosologic entity) may be included in a unitarian conception of the blood-forming system.

AUTHOR'S SUMMARY.

MODIFICATIONS OF THE CAPILLARY RESISTANCE IN ABDOMINAL LEISHMANIASIS OF CHILDREN. G. MACCIOTTA, Riv. di clin. pediat. **31**:1294 (Nov.) 1933.

Macciotta reports eleven cases of abdominal leishmaniasis in children. He made observations as to the cause of the purpura and hemorrhages found in this infection.

The blood platelets were diminished from a normal count of from 300,000 to 400,000 to about half that number; there was lengthening of the bleeding time to six or eight minutes (normal, from three to four minutes); the clotting time was also lengthened; the retraction of the clot was definitely delayed.

The arterial blood pressure is low in leishmaniasis and falls as the intensity of the symptoms increases. The blood capillaries are uniformly dilated, and their permeability is increased; they are also more fragile than normal capillaries.

Hemorrhages would doubtless be more common in leishmaniasis if the intracapillary pressure were not so low.

HIGGINS, Boston.

ALTERATIONS IN THE MINERAL CONTENT OF THE BLOOD OCCURRING IN SERUM ANAPHYLAXIS. D. CORDA, Riv. di clin. pediat. **31**:1409 (Dec.) 1933.

Corda made observations on the content of calcium, magnesium, phosphate, sodium and potassium in the blood serum of guinea-pigs before and during anaphylactic shock produced by horse serum. Similar observations were made on children during the stage of serum sickness and following recovery. The serum produced in almost every case a definite fall in the blood calcium (average for children, 2.5 mg. per hundred cubic centimeters) and in the blood phosphorus (1 mg.). There was usually a slight fall in the blood magnesium. On the other hand, there was usually a definite rise in the blood potassium (average, 3 mg.) and in the blood sodium (average, 180 mg.).

HIGGINS, Boston.

A CASE OF LIPOID NEPHROSIS. G. VIDAL JORDANA and J. MARCH GODAY, An. de pediat., Barcelona **1**:9 (Jan.) 1934.

A child aged 4 years had edema of the extremities, a low grade temperature, anorexia and albumin, white cells and some erythrocytes in the urine. In the laboratory findings the Mantoux reaction with a 1:1,000 dilution was intensively positive. Urinalysis showed albumin (6.6 Gm. per thousand cubic centimeters). Examination of the blood showed: serum, 15 per cent; globulin, 85 per cent; viscosity, 1.8, and sedimentation, 120 mm. The venous tension was 19 cm. of water, and the arterial tension, 11/6.5. The various aspects of this condition are discussed in detail, and a good bibliography is given.

SANFORD, Chicago.

EMBRYONIC ADENOSARCOMA IN CHILDHOOD. LEON VELASCO BLANCO, MARCELO E. ECHEGARAY and OSCAR BEHR, Arch. am. de med. **9**:87 (July) 1933.

The authors report this condition in a child 4 years old. The tumor occupied the entire left side. Its size made splenic or renal differentiation impossible. At

operation the tumor was found to involve the entire left kidney and was of the embryonic adenosarcoma type described by Birch-Hirschfeld. Surgical procedure is the only treatment indicated. The outcome is generally fatal, although Steffen reported eighteen recoveries in a series of eighty-eight cases.

SCHLUTZ, Chicago.

URINARY LITHIASIS IN CHILDHOOD. GENEROSO A. SCHIAVONE, Arch. argent. de pediat. **3**:812 (Dec.) 1932.

The author reports a case of this condition in a boy 10 years old. A vesical calculus the size of a hen's egg was found in the bladder and was removed by suprapubic operation. The child has been remarkably free from symptoms.

SCHLUTZ, Chicago.

TWO CASES OF ANEMIA DUE TO WORMS; TREATMENT BY IRON. G. G. ROMEIRO and P. BRAZIL, Arch. de pediat., Rio de Janeiro **6**:541 (Feb.) 1934.

Both the patients showed a continued drop in hemoglobin and red cells while being treated with antihelminthics, but an immediate rise following medication with iron.

SANFORD, Chicago.

SEVERE ANEMIAS OF CHILDHOOD. A. CARRAU and R. ETCHELAR, Arch. urug. de med., cir. y especialid. **2**:641 (May) 1933.

Four forms of anemia are discussed:

1. Von Jaksch's anemia, an intense type, with splenomegaly, hepatomegaly, erythroblastosis, leukocytosis and other symptoms. This appears in infants living in poor environments, who have suffered from digestive and nutritional upsets and who have more or less severe rickets; many of these have congenital syphilis or have had contact with tuberculous patients. Von Jaksch's anemia is rare in Spain. Five cases are reported, in three of which the patients died. Treatment consisted of blood transfusions, the administration of iron and liver and therapy for gastric disorders.

2. Splenic anemia and sickle cell anemia. Two cases in sisters are reported. Both patients became ill at the same time and received the same treatment of sulpharsphenamine, liver and ultraviolet ray therapy, yet one died, while the other lived.

3. Aplastic anemia. Five cases are reported which are typical in that the patients presented marked anemia, with achromia, erythroblasts, poikilocytosis, anisocytosis, marked leukopenia with a predominance of lymphocytes and a marked reduction in the platelets. The cases were in infants from 5 to 15 months of age, four of whom were boys. All died. Treatment consisted of the administration of liver, iron, blood, arsenic and other therapeutic agents, all of which were of no avail.

4. Syphilitic febrile anemias with erythroblastic reaction. Two cases are reported in both of which the patient died. Both patients had congenital syphilis, were malnourished, asthenic and febrile and had splenic and hepatic enlargement. The blood picture showed an index of more than 1, leukocytosis, normal platelets, erythroblastosis, poikilocytosis and anisocytosis. The treatment was the same as that described previously.

HERRON, Spokane, Wash.

AN ANATOMIC STUDY OF FOLLICULAR ILEOCOLITIS OF CUBA. AUGUSTIN CASTELLAMOS, Bol. Soc. cubana de pediat. **5**:173, 1933.

The similarity of the pathologico-anatomic lesions of bacillary dysentery in foreign countries and the enterocolitis of Cuba is impressive. Castellamos found on the basis of his experimental work that the pathogenesis is apparently the same. The causative agent is not clearly established in any of the forms.

SCHLUTZ, Chicago.

NEW VARIETY OF COLIC STASIS. MARTINEZ VARGUS, Med. de los niños **35**:161 (June) 1934.

Two cases of intestinal obstruction are reported in which anatomic defects were demonstrated. The familial character of stasis of the colon is emphasized. The principal symptoms in partial obstruction are periodic vomiting, small stools, headache and the presence of a palpable mass. The article describes the various causes of incomplete intestinal obstruction, the importance of the test meal with carmine and roentgen examination of the bowel to determine the location and extent of the obstruction.

DWYER, Kansas City, Mo.

FALSE PULMONARY ROENTGEN IMAGES. LUIS CARRASCO FORMIGUERA, Paidoterapia **12**:781 (Dec.) 1933.

The author reports a case of pulmonary tuberculosis with a primary complex in the apex of the left lung that was at first thought to be a cyst on roentgen examination. He emphasizes the fact that the roentgen rays are of value only when used in correlation with the clinical picture. The case was that of a child aged 4 years with fever and a cough. The Pirquet reaction was positive. A roentgenogram revealed a localized shadow in the apex of the left lung and peribronchial infiltration. The first diagnosis was a pulmonary cyst. The next roentgenogram, taken more than a year later, showed absence of the peribronchial infiltration, but the apical shadow remained about the same. The third roentgenogram, taken eighteen months later, showed a calcified Ghon tubercle. No results of clinical examination of the chest are presented.

HERRON, Spokane, Wash.

DIAPHRAGMATIC DISORDERS IN INFANTS AND CHILDREN. ISAAC A. ABT, Paidoterapia **12**:875 (Jan.) 1934.

The anatomy of the diaphragm is reviewed, and then the function of this muscle, which, next to the heart, is considered the most important muscle in the body, is described.

Inflammation of the diaphragm is nearly always secondary to involvement of abdominal or thoracic organs. Waxy degeneration often follows pneumonia. The phrenic, intercostal, sympathetic and vagus nerves are discussed. The movements of the diaphragm in respiratory diseases were amply studied, and the phenomenon of Williams, paradoxical movements, the influence of pneumothorax on its mobility and other features are discussed. Interesting observations were made on the tonic and clonic spasms of the diaphragm. Subdiaphragmatic abscess is discussed in detail, as is diaphragmatic hernia. Five cases of the following conditions, respectively, are reported: a hump in the center of the right diaphragm, which was discovered accidentally; elevated position of the left diaphragm following pneumonia and pleurisy; subphrenic abscess; relaxation or eventration, and diaphragmatic hernia.

HERRON, Spokane, Wash.

ETIOLOGY AND TREATMENT OF DYSENTERIFORM ENTEROCOLITIS IN THE FIRST TWO YEARS OF LIFE. N. SPYROPOULOS, Paidoterapia **12**:1113 (March) 1934.

In order to call the diarrhea dysenteriform the stools should contain mucus and blood. The disease is a disorder (not infection) of the gastro-intestinal tract caused not by specific organisms but by other means, such as atmospheric temperature and extreme changes in the diet. The author found that 9 per cent of infants from 1 to 6 months of age, 50 per cent from 6 to 12 months of age and 32 per cent from 12 to 18 months of age have this disease. In a series of 172 cases the apex was reached in June, and in practically 85 per cent of the cases the disorder occurred during the late spring, summer and early autumn.

The author believes the principal cause of enterocolitis to be not bacterial but due to improper feeding. This produces dyspepsia, first in the stomach, then in the intestine. This "food poisoning" of the intestine is the sole cause of dysenteri-

form enterocolitis in the first two years of life in the first phase of such illness. The second phase is characterized by the entrance of various micro-organisms and intestinal parasites. The author found Bacillus coli in 92 per cent of the cases, the Shiga-Flexner bacillus in 2 per cent and other cocci in 6 per cent.

Dysentery serum showed no influence on the course of the disease, and hence the disease did not proceed from agents of dysentery. The development and termination of the illness depend on the treatment.

Treatment consists of a mild laxative and the stopping of all food by mouth for twenty-four hours. Fluids are given parenterally on the first day; on the second day rice water (two glasses) is given. On the third day one or two glasses of vegetable broth are given, and then sugar water is started in small amounts, calcium caseinate being added. Fat-free milk may be used. Concentrated breast milk is added later. The author does not compare the incidence of the disease in the breast fed and the artificially fed infant.

HERRON, Spokane, Wash.

HEADACHES OF THE SCHOOL CHILD. TORELLO CASANOVAS, Paidoterapia **12**:1237 (April) 1934.

The frequency with which the author, an ophthalmologist, observed headaches in children brought forth this study.

The causes, in addition to refractive errors, include nervous fatigue due to overwork in the classroom; heredity; organic intracranial lesions, such as tuberculosis, syphilis, hydrocephalus and tumors; endocrine disturbances; adenoids and tonsils; poor ventilation; digestive upsets, and deficient lighting.

HERRON, Spokane, Wash.

PRECOCIOUS ACROMEGALY AND JUVENILE KYPHOSIS. F. RODRIGO PALOMARES, Pediatría españ. **22**:449 (July) 1933.

This rare disorder was observed by the author in a girl 10 years old. Four other children in the family and all the antecedents were well. The general development of the child was massive, and there was a heavy panniculus. The features were large, and the facial expression was dull and languid. The lips and tongue were large and the teeth irregular and much decayed. The voice was thick, and speech was scanning. Sexual development was markedly retarded. The girl had the mental age of a child of 8 years. Vision was fairly normal. The Wassermann reaction was negative and the Pirquet reaction positive. A roentgenogram of the skull showed a markedly enlarged sella turcica. The vertebral bodies of the spinal column showed considerable deformity and lack of calcification, the condition resembling the pathologic osseous picture seen in rachitis tarda.

The author believes that hypertrophy of the pituitary gland explains both the acromegalic and spinal condition. Hypertrophy of the gland can lead to either a condition of hyperpituitarism or the condition in this case, namely, hypopituitarism.

SCHLUTZ, Chicago.

HEPATIC ABSCESS OF AMEBIC ORIGIN IN A CHILD AGED THREE AND ONE-HALF YEARS. B. R. ALDUNATE, Rev. chilena de pediat. **4**:155 (April) 1933.

This unusual condition in so young a child was treated by repeated aspiration and the use of emetine and acetarsone (stovarsol) and resulted in complete cure. The pus in the abscess was sterile, but the amebas were found in the wall of the abscess cavity. There was no dysentery. According to the author, this may be absent in abscess of the liver due to ameba.

SCHLUTZ, Chicago.

THERAPY OF PRURITUS ANI. FRANZ HAMBURGER, Arch. f. Kinderh. **101**:117 (Jan. 31) 1934.

For prolonged and resistant cases of pruritus ani in children Hamburger suggests the following sedative and antispasmodic ointment to be used locally in the

evening: extract of laudanum, 0.01 Gm.; atropine sulphate, 0.002 Gm.; oil of bergamot, 2 Gm.; hydrous wool fat, 9 Gm., and petrolatum, 9 Gm.

LEMASTER, Evanston, Ill.

CLINICAL AND EPIDEMIOLOGICAL ASPECT OF PNEUMONIA: I. CLINICAL COURSE AND PNEUMOCOCCIC TYPE. I. OETTINGER, I. MASEL and L. WIKTOROW, Deutsches Arch. f. klin. Med. **174**:602 (Feb. 9) 1933.

This aricle is an extensive analysis of 361 cases of lobar pneumonia occurring in Moscow. Type I Pneumococcus caused 41 per cent of the cases; type II, 16.5 per cent; type III, 9.5 per cent, and group IV, 33 per cent. Infection due to type I was more common in young persons, that due to type III in older ones. In cases with a sudden onset, continuous fever and a definite crisis the condition was usually due to type I, whereas in the atypical cases the disease was usually due to type III. Bacteremia appeared in 25 per cent of all the cases and was accompanied by a 36 per cent mortality. The mortality in cases with sterile blood cultures was only 1.3 per cent. Complications were more frequent in infections due to type I. There seemed to be little variation in the duration of the illness among the various types. A study of the localization showed the usual predilection for the two lower lobes of the lungs, which was especially marked in infections due to type I and group IV.

DOOLEY, Kent, Conn.

CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF PNEUMONIA: II. TYPE-SPECIFIC REACTION OF URINE. I. OETTINGER, I. MASEL and L. WIKTOROW, Deutsches Arch. f. klin. Med. **174**:615 (Feb. 9) 1933.

The authors found a higher percentage of positive precipitin reactions (90 per cent) than has been reported hitherto. (Avery reported 65 per cent positive reactions in cases of pneumonia.) The early appearance of a positive precipitin reaction is considered an unfavorable prognostic sign. Reactions are recorded for 105 cases of lobar pneumonia, which were classified as follows: type I, 46; type II, 26; type III, 12, and group IV, 21.

DOOLEY, Kent, Conn.

CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF PNEUMONIA: III. SIGNIFICANCE OF CARRIERS IN THE SPREAD OF TYPE I AND TYPE II PNEUMONIA. I. OETTINGER and L. WIKTOROW, Deutsches Arch. f. klin. Med. **174**:620 (Feb. 9) 1933.

Studies were made of the flora of the nose and throat in several groups of persons in an effort to learn the incidence and variety of Pneumococcus present.

Among 308 persons who had had no known contact with patients with pneumonia, Pneumococcus was present in 54 per cent, with the following distribution: type I, 0; type II, 1.2 per cent; type III, 11.9 per cent, and group IV, 86.9 per cent. In 361 cases of lobar pneumonia Pneumococcus showed the following distribution: type I, 41 per cent; type II, 16.5 per cent; type III, 9.5 per cent, and group IV, 33 per cent. Nearly half of 77 relatives of 19 persons with type I or type II lobar pneumonia had positive cultures. The organism was divided as follows: type I, 8.9 per cent; type II, 16.1 per cent; type III, 8.9 per cent, and group IV, 66.1 per cent. Carriers in this group were three times as frequent as in a group of 186 hospital employees who were in contact with the same patients.

Pneumococcus types I and II usually disappeared during the first or second month of convalescence after lobar pneumonia.

DOOLEY, Kent, Conn.

THROMBOSIS AND PHLEBITIS OF THE SPLENIC VEIN IN CHILDHOOD; ("STENOSIS OF THE SPLENIC VEIN"). E. NOBEL and R. WAGNER, Ergebn. d. inn. Med. u. Kinderh. **45**:1, 1933.

Thrombosis of the splenic vein as a cause of splenomegaly stands out as a definite symptom complex among the other splenomegalies of childhood, but it

appears to have its greatest resemblance to the Banti syndrome. Although the condition is rare, nevertheless the symptoms are definite, and the prognosis subsequent to the proper treatment is so much better than in some of the other splenomegalic symptom complexes that it appears justifiable to analyze the condition in some detail.

The symptoms of thrombosis of the lienal veins are explicable on an anatomic basis. When the emptying of the splenic veins is blocked, a collateral circulation is established. The veins in the phrenicolienal and gastrolienal ligaments dilate and bring about a connection with the vena cava superior through the esophageal veins or with the portal vein through the coronary veins of the stomach. In stasis of the portal vein a collateral circulation can also develop through connection between the inferior mesenteric vein and the hemorrhoidal veins with the inferior vena cava. As a result of the rupture of a varix in the collateral circulation the hemorrhages characteristic of stenosis of the splenic vein come about.

Nobel and Wagner report in some detail two of their cases, in one of which the patient was cured by splenectomy, while the other patient, who was treated by medical instead of surgical means, is still under observation. They also append a table giving a brief résumé of twenty-five other cases of thrombosis of the splenic vein in children, which has appeared in the medical literature.

They cite the causes of thrombosis of the splenic vein, as given by A. Weinert, as follows: (1) various peritoneal pathologic processes affecting the outer walls of the veins through compression by enlarged lymphatic glands or pancreatic disorders; (2) infections; (3) splenitis; (4) processes of degeneration in the walls of the veins, which lead to sclerosis, and (5) trauma.

There are three chief symptoms that characterize stenosis of the lienal vein; (1) hematemesis, (2) anemia and (3) splenic tumor. The latter exhibits a peculiar fluctuation in size, in that the spleen diminishes in size after the hematemesis and enlarges during the interval that is free from bleeding. The block in the splenic vein brings about a circulatory disturbance which, on the one hand, causes venous stasis in the spleen with hypertrophy of the latter, and, on the other hand, the development of a collateral circulation. The splenic artery continues to bring new blood into the spleen, which must be carried off by new routes. This is brought about through an anastomosis with the gastric and esophageal veins and also between the veins of the splenic capsule and those of the diaphragm. These veins continue to dilate more and more and may even become thrombosed in their course. As the impediments in the circulation increase, varices finally develop in the esophageal and gastric veins, which on rupturing lead to hematemesis.

The anemia is of the secondary type during the interval, and the majority of cases exhibit leukopenia; however, immediately after a hemorrhage all the phenomena that usually follow a severe loss of blood occur, namely, very low values for hemoglobin and red blood cells, the appearance of nucleated red cells and the development of leukocytosis; the thrombocytes likewise seem to reach normal values after a hemorrhage, only to show a tendency to thrombopenia during the interval.

The finding of a splenic tumor in association with anemia is a not uncommon symptom complex in children. On the other hand, fluctuations in the size of the spleen (as they are seen in thrombosis of the splenic vein) are hardly ever manifested in splenomegaly due to other causes in childhood. The lower border of the spleen during intervals is mostly several fingerbreadths below the costal margin, is firm and smooth and usually exhibits no notch. Pain or a feeling of pressure in the splenic area depends on the size of the spleen and the rapidity with which it enlarges. Immediately after a hemorrhage the edge of the spleen may be just barely palpable under the costal margin.

Besides the three main aforementioned symptoms, there may be a few less characteristic and constant ones, namely, ascites, which may be slight, transient and inconstant (in contradistinction to cirrhosis of the liver); it is only slight if there is enlargement of the liver with no disturbance in hepatic function. Occasionally esophagoscopy or, better still, roentgenologic examination of the esophagus

may give additional evidence of the existence of varices and thus aid to establishing the diagnosis.

In the differential diagnosis Nobel and Wagner discuss gastric ulcer, hemorrhagic diseases, various infectious diseases that are accompanied by splenomegaly, aleukemic leukemia, syphilis, Gaucher's and Niemann-Pick's disease and, particularly, Banti's disease; stenosis of the splenic vein resembles most closely the latter.

They make the final statement that "in the course of an investigation of a child who gives a history of repeated attacks of hematemesis, in whom gastric or duodenal ulcer has been excluded, and who shows a rapidly enlarging spleen subsequent to a recent attack of hematemesis, one must invariably consider the diagnosis of stenosis of the splenic vein."

Treatment consists in relief of the symptoms of the secondary anemia by means of iron therapy and blood transfusions or in radical measures, namely, splenectomy. In employing transfusions soon after a hemorrhage one must not use too large a quantity of blood, or another hemorrhage may follow from the same site of the preceding area of bleeding. This took place in one of the authors' cases. It is conceivable that as a result of the canalization of the thrombus spontaneous cure may occur. In most cases, however, a radical cure of the circulatory block can be effected only through splenectomy. The operation is less dangerous and is attended by a greater measure of success in children than in adults. Wallgren reports that of six children on whom splenectomy was performed one was unimproved, whereas among five adults who were operated on three died. The authors' patients who had been operated on were still free from a recurrence of symptoms five years after splenectomy.

CAPPER, Philadelphia.

RENAL DWARFISM WITH AND WITHOUT RENAL RICKETS. H. HAMPERL and K. WALLIS, Ergebn. d. inn. Med. u. Kinderh. **45**:589, 1933.

In studying cases of undisputed renal rickets Hamperl and Wallis found dwarfism in practically all of them. Regarding the influence of infections on the occurrence of the renal disorder in this symptom complex, they express the belief that either it is purely a coincidental occurrence or that the acute infections in a nonspecific manner aggravated and brought to light hitherto latent and chronic nephritis. The signs of chronic nephritis encountered in about half of the cases were polyuria and polydipsia; the urine showed a low specific gravity, and the concentration capacity of the kidneys was decidedly damaged. Hypertension and hypertrophy of the heart, which are the usual findings in cases of contracted kidneys, are relatively rare in renal rickets and renal dwarfism; among sixty-nine cases of renal rickets, clinical or postmortem evidence of moderate cardiac hypertrophy, especially of the left ventricle, was found in fifteen cases, and a rise in blood pressure in only sixteen. Corresponding to the usually observed pallor of the skin, one finds in most cases definite anemia of the hypochromic type. The blood calcium and phosphorus determinations are of the same level in renal rickets as in simple nephritis; with an increase in the blood urea the calcium-phosphorus quotient is regularly lowered, only to be increased again with improvement in the general condition and restoration of the normal blood urea. Not only is there a definite rise in the urea and nonprotein nitrogen during the uremic stage of renal rickets, but a definite relationship exists between the rachitic bone processes and the rise in the blood nitrogen, so that with a remission in the osseous phenomena the blood nitrogen is definitely lowered. In renal dwarfism, as well as in renal rickets—just as in ordinary nephritis—there is a tendency toward acidosis, particularly during the uremic stages.

The osseous phenomena of renal rickets resemble strikingly those of pure classic rickets. There appear more or less definite enlargements of the epiphyses of the long bones, rosary, Harrison's groove, sometimes prominent frontal bosses and, in young children, delay in the closure of the anterior fontanel and bowing of the long bones, with genu valgum more often than genu varum.

Parsons and Teall described three roentgenologic types: (1) the atrophic type, in which the whole bony skeleton is fragile, atrophic and osteoporotic; (2) the type resembling florid rickets, in which the epiphyses resemble those seen in classic rickets but in which the atrophy and fragility of the long bones are not as striking as in type 1, and (3) the honeycomb type, which, according to Parsons and Teall, is particularly characteristic of renal rickets. This type received its name from the peculiar changes in the widely dilated metaphyses, which have a mottled and moth-eaten appearance. The failure of calcification of the epiphyses of the carpal bones cannot be ascribed to the renal rickets, but rather to the associated dwarfism. In contradistinction to classic rickets, in renal rickets there is rarely damage of the dental enamel or caries. Renal dwarfism does not necessarily occur with renal rickets, whereas in practically all cases of renal rickets there is associated dwarfism; Hamperl and Wallis found an exception to the latter findings in only six of the sixty-nine cases. The fact that there are reports in the literature of twenty-five cases of renal dwarfism without any demonstrable rickets leads one to conclude that the dwarfism is not the result of rickets; the small stature simply represents a cessation or delay in growth rather than a rachitic pathologic condition. Similar to the delay in the bone growth, there was also a decided lag in the body weight, an average of 40 per cent, according to the authors' calculations. However, if one figures weight for height, there was no decided degree of underweight, either in cases of renal rickets or in those of renal dwarfism. The interesting fact is brought out that in a surprisingly large number of cases the disturbances of growth occurred very early, and often the smallness of the child was observed at birth.

The mental development of children with this condition is usually normal, and occasionally they even appear to be especially intelligent, although a number of authors speak of the unfavorable prognosis in renal rickets or renal dwarfism. Practically all the patients die from kidney disease, although occasionally spontaneous recovery has been reported. In most cases the cause of death has been given as uremia associated with acidosis and a marked rise in the blood urea; convulsions as a terminal result have been reported in only a few cases. The treatment is chiefly dietary with a view to relieving the kidney disease. The differential diagnosis between a case of typical renal dwarfism with chronic interstitial nephritis and a case of mere delay in growth associated with renal disease is aided by the appearance of signs of renal rickets, and occasionally only the observations at autopsy lead to the final decision. An absolutely negative history as regards preceding acute nephritis may be utilized as a point in favor of renal dwarfism.

In discussing the pathologic anatomy of this condition, Hamperl and Wallis state that in all but one of the undisputed cases of renal rickets in which the kidneys had been examined histologically chronic interstitial nephritis was found. They conclude, therefore, that in the vast majority of cases of sure renal rickets a peculiar type of contracted kidney of unknown etiology is found which is distinguishable from the hitherto recognized form of contracted kidney and which may be classified as chronic interstitial nephritis. In contradistinction to Mitchell, these authors assert that in every sure case of this particular form of nephritis there is associated renal rickets or renal dwarfism; they explain Mitchell's two cases of nephritis without renal rickets or dwarfism by stating that, in the first place, Mitchell is one of those who consider every increase in renal interstitial connective tissue as chronic interstitial nephritis and, in the second place, in one of Mitchell's cases there was also associated arteriosclerosis, and that this case may, therefore, possibly have been one of arteriosclerotic nephritis.

Pathologically, the osseous changes in renal rickets belong to the sphere of rachitis tarda, yet the authors could not find a single case in which it could be maintained with certainty that the renal rickets was influenced favorably by the use of antirachitic measures. That the rachitic condition did not result from the nephritis is supported by the clinical experience that the development of typical renal rickets secondary to chronic nephritis is the exception rather than the rule.

CAPPER, Philadelphia.

CONGENITAL EPIDERMOID CYST OF THE HEART. A. DE CHATEL, Frankfurt. Ztschr. f. Path. **44**:426, 1933.

In a new-born girl a cyst of the interauricular septum was found, which on histologic examination appeared to be a multilocular dermoid cyst containing derivatives of the three germinative layers. De Chatel was unable to find record of a similar case in the literature. He is inclined to explain the dermoid cyst on the basis of misplaced ectodermal cells or on that of metaplasia of entodermal cells in a very early stage of development. A meningo-encephalocele and a defect of the nasal septum were also found at autopsy.

WILLIAM SAPHIR, Chicago. [ARCH. PATH.]

TREATMENT OF THE CHILDHOOD TYPE OF DIABETES. L. R. GROTE, Kinderärztl. Praxis **4**:153 (April) 1933.

Grote writes with the authority of ripe experience in the treatment of diabetes in the Von Noorden clinic. In about 25 per cent of the cases heredity is an etiologic factor. Infection—not so much the exanthems as acute infection of the upper respiratory tract and parotitis—is a not unimportant exciting cause. The disturbance of metabolism in the childhood form of diabetes differs from that of the adult form only in its intensity. The glycogen poverty of the liver and the insufficiency of glycogen fixation are more pronounced; this accounts for the long continued hyperglycemia, the tremendous glycosuria and the ketosis. Children are never resistant to insulin, as the arteriosclerotic type of adults are, but, on the contrary, are much more frequently sensitive to this substance, the insulin working too well and resulting in hypoglycemia.

Grote maintains that the optimal number of calories for a growing child is 100 per cent above its basal metabolism requirements, although Joslin prescribed only 50 per cent. Thirty per cent of the total calories should be carbohydrate (as much as possible of this in the form of fruit). The amount of protein varies from 3 Gm. per kilogram of body weight in a very young child to 1 Gm. per kilogram in a 15 year old child.

The initial treatment of diabetes is best undertaken in a special institution for diabetic patients, because the blood sugar should be determined every hour and the urine examined not less often than every two hours. Only patients with the mildest cases can get along on a single daily dose of insulin. The majority of patients require two doses, of which the morning dose is one third larger. Many patients do better on three doses, of which the midday portion is the smallest; only the youngest children require four doses. Acidosis occurs only with infection or when an insufficient amount of insulin has been given. In the treatment of acidosis the amount of insulin is regulated by hourly determination of the urinary sugar or the blood sugar. The diet consists of oatmeal, rice and fruit or, in appropriate cases, pure fruit juice. In severe cases a liter of physiologic solution of sodium chloride should be given by hypodermoclysis, coincidentally with the first injection of insulin, which should be given intravenously. Even in children as much as 200 units of insulin may be given in twenty-four hours.

The prognosis of diabetes is not dependent on the age of onset; even in infants the prognosis may be good. In comparing the treatment of diabetes today with that in preinsulin days, Grote is optimistic. One is not only able to preserve the lives of diabetic patients but can promise them useful and happy lives without undue hardships.

HUENEKENS, Minneapolis.

EXPERIMENTAL CONTRIBUTION TO ALKALI THERAPY. Z. STARY and P. MAHLER, Med. Klin. **29**:1509 (Nov. 3) 1933.

The volume of gastric secretion, when alkali is given simultaneously with the test meal, is greatest after the administration of sodium bicarbonate, less after that of calcium carbonate and least after that of magnesium oxide. When alkali has

been administered previously there is a similar but somewhat reduced action. The chloride content of the secretion, at least at first, is reduced by sodium bicarbonate, increased by calcium carbonate and variously affected by magnesium oxide. Free hydrochloric acid returns soonest after the administration of sodium bicarbonate, but very late after that of the two other alkalis. In immersion experiments with excised human stomach it was found that calcium carbonate and magnesium oxide form a mucosal coating which may be presumed to serve as a sort of alkali depot.

DOOLEY, New York.

APHTHOID (POSPISCHILL). L. KUMER, Med. Klin. **30**:303 (March 2) 1934.

Kumer describes the case of a 2 year old boy who died fifteen days after being burned on the buttocks. On the second day there was a severe toxic exanthem on the trunk and extremities, and on the twelfth day lesions of the aphthoid type developed about the nose and mouth. These were thick-walled vesicles on a slightly infiltrated reddish base. They did not involve the oral mucous membrane, as they usually do in this condition. Reports of experiments on animals and clinical findings suggest an etiologic relationship between aphthoid eruption, herpes simplex and stomatitis aphthosa. Kumer inoculated the corneas of two rabbits with material scraped from the crusts. One animal died of encephalitis; in the other there was complete corneal healing, with subsequent protection against a highly virulent virus of the herpes type. It is suggested that the aphthoid eruption may be an ecthyma form of the otherwise harmless herpes simplex.

DOOLEY, New York.

CAUSE AND FREQUENCY OF ALBUMINURIA IN CHILDREN. HERBERT NOWAK, Monatschr. f. Kinderh. **59**:341, 1934.

During the years 1932 and 1933, Nowak examined 4,500 boys, aged 14 to 17. Orthostatic albuminuria with lordosis was present in 248 (5.5 per cent). Orthostatic albuminuria without lordosis was present in 276 (6.1 per cent). Chronic kidney trouble was present in 36 (0.8 per cent). Nowak next attempted to classify the subjects with lordosis and found that there was some relationship between the degree of lordosis and the severity of the symptoms. On the other hand, the absence of lordosis in so many cases led him to seek other causes, and he redivided the boys into another three groups: those with general muscular flaccidity and postural defects, those with special susceptibility to catarrhal infections with adenopathy and large tonsils and a miscellaneous group with neuropathic tendencies, dental caries and chronic disease of the middle ear. One hundred and forty-two fell in the first group, 77 in the second and 29 in the third.

In only two of the 36 cases of nephritis was there a history of previous orthostatic albuminuria.

Nowak concludes that lordosis is probably a definite cause of orthostatic albuminuria, but that the condition can be brought on by many other constitutional abnormalities that lead to changed circulation in the kidneys.

GERSTLEY, Chicago.

MASSIVE ANEMIC NECROSIS OF THE LUNG IN PNEUMONIA. M. REINISCH, Virchows Arch. f. path. Anat. **290**:75, 1933.

Reinisch reviews the small number of reported cases of pneumonia that terminated in massive anemic necrosis of the inflamed lung. The case which he reports is that of a 5 year old boy who became suddenly ill the middle of January with a characteristic attack of pneumonia. The temperature returned to normal on the tenth day, but rose again two days later. Admission to the hospital occurred on February 12, at which time there was flatness on percussion of the lower part of the thorax on the left posteriorly; breath sounds were absent in this region. On the next day half a liter of purulent exudate was removed from the left side

of the chest by thoracotomy. Death occurred on February 21. Necropsy revealed two relatively large, sharply defined areas of ischemic necrosis in the organizing upper lobe on the left. Reinisch divides the recorded cases of the condition into three groups. In the first two the essential factor is arterial thrombosis. The anemic character of the infarct is due to the inflamed state of the lung, which prevents the backflow of blood through the collateral capillaries. In the first group the lesion contains no bacteria, and the condition is termed aputrid anemic necrosis. In the second group bacteria are present; the condition is called septic anemic necrosis. In the third group, in which Reinisch places his own case, the essential factor is bacterial activity. Bacterial action causes thrombosis and necrosis; this condition is called septic necrosis. The justification for making a distinction between the second and third groups does not appear well founded.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

GENERALIZED DISEASE OF THE OSSEOUS SYSTEM IN CHILDHOOD. E. HÄSSLER and KRAUSPE, Virchows Arch. f. path. Anat. **290**:193, 1933.

A condition which was clinically diagnosed as aleukemic myelosis in a child, 27 months old, who presented, in addition, osteosclerosis and terminal anemia, is the subject of a comprehensive clinical and roentgenologic report by Hässler. For comparison he includes similar studies of a case of generalized sarcomatosis of the skeleton, with osteolysis and osteoporosis, two cases of osteitis fibrosa cystica and one of Albers-Schönberg disease, with active rickets, scurvy and anemia. All these conditions occurred in infants. Krauspe follows with a detailed histologic study of the bones in the case of aleukemic myelosis and in that of Albers-Schönberg disease. He interprets the first condition as primary hyperplastic disease of the bone marrow, with reactive osteosclerosis, which in turn led to anemia. In the case of Albers-Schönberg disease both the osseous system and the hematopoietic system were primarily involved. The case of marble disease described had some of the characteristics of von Jaksch's anemia. Krauspe gives also the results of a histologic study of the bones in two cases of lymphatic leukemia and in one case of myeloid leukemia in children. Although osteolytic and osteoporotic changes predominate in leukemia, there may be subperiosteal new formation of sclerotic bone.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

IS BLOOD PRESSURE DURING PHYSICAL EXERCISE INFLUENCED BY THE INTAKE OF FOOD? W. RAAB, Wien. Arch. f. inn. Med. **24**:161 (Nov.) 1933.

The liberal intake of food changes the systolic blood pressure in normal persons little and not in any characteristic manner. In hypertonic persons there is a tendency for the systolic pressure to decrease after the intake of food. The diastolic pressure sinks in both normal and hypertonic persons after the intake of food.

Physical exercise increases the systolic pressure, with few exceptions. This reaction is particularly pronounced in hypertonic persons. The diastolic pressure, however, declines in varying degree. The reaction of the systolic pressure following exercise is not changed essentially through the intake of food. The decline of the diastolic pressure is somewhat increased.

The subjective feeling of fatigue after the intake of food is referable not so much to changes in the peripheral vascular bed as to the increased demands on the heart on account of the increase of the minute volume.

SCHLUTZ, Chicago.

TREATMENT OF ANEMIA IN INFANTS. H. LEHNDORFF, Wien. klin. Wchnschr. **46**:784 (June 23) 1933.

Lehndorff states that alimentary anemia, or true anemia of nurslings, occurs only in the first year of life. It is caused by the absence of substances in the

milk which are necessary for the formation of erythrocytes or hemoglobin in the blood (iron, copper, amino-acids, vitamins, etc.). Most nurslings, though they may not appear anemic, have a low hemoglobin count. According to Helen Mackay (London), this drops from 95 per cent in the third and fourth weeks of life to less than 70 per cent in the second to the third month, remaining at this level until the end of the first year, with but slight variations. In bottle fed infants the curve may be from 5 to 6 per cent lower. In Austria this curve is somewhat higher, owing to the early addition of vegetables and fruit to the diet.

Iron is the most effective remedy for the hypochromatic chloro-anemias with a low hemoglobin content and a relatively high erythrocyte count. The more severe anemias react much better than the milder forms. Drugs have practically no effect in cases in which the hemoglobin content is over 70 per cent, and some drugs, such as arsenic, are harmful when the blood is normal. The age of the child is an important factor. According to Finkelstein, the infant becomes "ripe for iron" only toward the end of the first half year of life. At this time the appetite, weight, mood, sleep and muscular turgor all display striking improvement, as does the blood picture. In contrast to Finkelstein's conclusions, Mackay found that iron is effective from the first month of life; in fact, it serves as a protection against the anemia of premature children and raises the resistance to infections of all kinds. According to Finkelstein, iron acts as a catalytic agent, stimulating the sluggish bone marrow to heightened activity. It is best to administer ferrum reductum U. S. P.; infants usually tolerate from 0.1 to 0.5 up to 1 Gm. daily well; these large doses cause diarrhea only infrequently. Since ferrum reductum is effective only when changed to ferrochloride by the action of gastric acid, it is advisable, because of the hypo-acidity of anemic children, to add hydrochloric acid (from four to five teaspoonfuls daily of ferrochloride, 2 Gm. in a solvent of 1 per cent hydrochloric acid, 200 cc.). Lemon juice or lactic acid may be used in place of the dilute hydrochloric acid. Copper, like liver, seems to act more on the erythrocytes than on the formation of hemoglobin. One or two teaspoonfuls of a preparation of copper sulphate, 0.5 Gm.; aqua, 1,000 cc. may be given in the milk three times per day; at the same time from 0.1 to 0.4 Gm. of ferrous carbonate per day (Lewis) is given. One-tenth per cent copper and 1 per cent iron preparations are valuable. The injectable liver preparations have little effect on infants. It is best to use fresh calves' liver (from 10 to 15 Gm. per kilogram of body weight). Stomach preparations have not yet been sufficiently tried out in cases of infants, and reports in the literature concerning them contradict one another.

Mild cases of anemia in infants do not require the use of arsenic, but it should be given to older children. Acetarsone stimulates the appetite and brings about a gain in weight; however, it does not affect the blood picture. Dietetically, the basic principles of Czerny should be followed: a diet low in milk, early and sufficient addition of fruit and vegetables to the diet and liver or meat daily.

Rickets may be prevented by the administration of cod liver oil and viosterol and by ultraviolet irradiation. In severe cases of anemia, blood transfusions may save the lives of patients. This procedure, especially in infants, should be conducted in the hospital. Intramuscular injections of 5, 10 or 20 cc. of blood from a vein of the mother, transferred immediately, body-warm, into the infant, are often beneficial.

ABT, Chicago.

CELIAC DISEASE. RICHARD PRIESEL, Wien. klin. Wchnschr. **46**:947 (July 28) 1933.

Priesel states that the syndrome of celiac disease embraces the following symptoms: typical bulky stools, a large fluctuating abdomen, hydrolability, disturbance of growth, osteopathy, diminished tension, anemia and characteristic metabolic disturbance (demineralization and intermediate acidosis). Fanconi, following a proposal of Feer, distinguished two major forms of Herter's intestinal infantilism with the typical celiac syndrome—the primary and secondary forms. The primary forms are due to inner constitutional causes in the sense of congenital

insufficiency of the digestive organs. Exogenous causes are secondary. Severe disorders of the small intestine exist in these cases, leading to the appearance of the syndrome of celiac disease, either during the first few months of life or in later childhood, with severe symptoms. Constitutional causes may be of some account in the secondary forms, but exogenous factors are the chief ones. According to Fanconi, these are: a spare diet continued over too long a period, severe rickets, anemias, ascarides and abdominal tuberculosis. This division by Fanconi has a practical significance, as the primary forms of Herter's infantilism, in which the constitutional factors predominate, require stronger therapeutic measures than the secondary forms, in which at least the exogenous causes may be removed by commensurate etiologic treatment. Thus Fanconi accomplished successful treatment in secondary forms of celiac disease following ascarides through application of a cure for worms. The Vienna Children's Clinic treats patients with celiac disease according to the nutritive principles outlined by Fanconi. At the beginning of treatment, especially of younger children, as well as in intermittent relapses, the patients are given a nutritive preparation containing only one half the whey and lactose of cow's milk, and, concurrently, calcium carbonate administered internally. Soon after, fruit juices and fruit, especially bananas, are added, and with improvement of appetite vegetables are given. It is difficult to adhere strictly to a prescribed scheme of diet, but the chief aim should be to find one which corresponds with the demands of a complete diet. Therefore, in spite of Fanconi's demand, fats, carbohydrates and even sugar are not to be withheld for a long period. The results of this dietary therapy, which was originally worked out by Schick and Wagner, have been gratifying. The diet, which is rich in calories, gives favorable results, unless intermittent infections, such as influenza and pneumonia, threaten the lives of the children with Herter's infantilism. It is important that the dietary regimen, once begun, should not be discontinued because of occasional threatening conditions in the stools. A child with a severe form of Herter's disease should not be too readily dismissed from the hospital. Dismissal should be permitted only after a favorable increase in weight and after the stools have improved considerably.

ABT, Chicago.

INFLUENCE OF HORMONE THERAPY ON THE DEVELOPMENT OF INFANTILE TYPES. W. GERSON, Ztschr. f. Kinderforsch. **42**:1, 1933.

Hormone therapy can bring about the development of body and character in infantile types or can increase the rate of this development so that the children recover from a delay of several years within a relatively short time. Not only infantile symptoms disappear, but even such symptoms as appear to be psychopathic. Most of the cases observed by the author were due to disturbances of the hypophysis. The greater the difference between the age and development the more justified is the use of hormone therapy.

REICHLE, Cleveland.

JUVENILE DIABETES IN THE LIGHT OF RECENT BIBLIOGRAPHIES FOR THE PAST TEN YEARS, AND PERSONAL OBSERVATION BY THE AUTHOR FOR THE PAST SIX YEARS AT THE PEDIATRIC CLINIC IN LWOW. A. CHWALIBOGOWSKI, Pedjatrja polska **13**:59, 1933.

An extensive résumé on diabetes mellitus in children is given. Little was known about this condition until insulin was discovered. In the discussion of the etiologic factor, Chwalibogowski comes to the conclusion from his observation and analysis of the cases that endogenous factors play a great part in the production of juvenile diabetes; that is, claims that diabetes is a hereditary disease.

In the analysis of his cases he found that children of all classes are afflicted with the malady. There is a slight preponderance in boys and in the Jewish race.

KRUPINSKI, Chicago.

HEMOLYTIC JAUNDICE IN A CHILD. I. KOBAYASHI, J. Pediat. (Tokyo), Nov. 20, 1933, no. 402, p. 2016.

A comparatively rare condition of hemolytic jaundice in a 5 year old child is recorded. This was sporadic and congenital, with no hereditary or familial background. The size of the spleen varied from day to day and did not run parallel with the intensity of the jaundice. Lymphocytosis, however, seemed to parallel the degree of jaundice. There was a marked increase in the fragility of washed corpuscles against hypotonic salt solution, which, however, did not parallel the degree of icterus. The liver showed a slight degree of dysfunction.

KATO, Chicago.

ACUTE PANCREATOGENOUS FATTY DIARRHEA IN A BOY AGED 10 YEARS. E. GJÖRUP, Acta pædiat. **15**:82 (Nov. 6) 1933.

This is the report of a case of a boy, aged 10 years, with a family history of tuberculosis. From a state of relative good health he fell ill suddenly with an acute exanthematous infection associated with fever and followed by generalized furunculosis, bilateral suppurative otitis media and diarrhea. For a time the stools contained blood, but no pathogenic organisms were demonstrated by culture. Subsequently the diarrhea assumed a spruelike character. Low-grade fever persisted; emaciation was progressive, and decubital infection developed. The Widal agglutination reaction, the Wassermann reaction and the tuberculin reaction were negative.

In the seventh month of the illness a metabolic study of the patient's fat and nitrogen balance was conducted. Only the stools were analyzed; urine was not collected. The intake of fat and nitrogen was determined by calculation. This study demonstrated what the author regards as an abnormally elevated excretion of ingested fat (52.3 per cent) and an increased output of nitrogen (ingested nitrogen, 12.04 Gm. daily; nitrogen in the stools, 3.05 Gm. daily). At the same time, when the patient was given orally 50 Gm. of dextrose (actual weight, 17.3 Kg.; calculated weight, from 26 to 28 Kg.), he showed glycosuria and a diabetic type of blood sugar curve. Gastric achlorhydria was present. The urinary diastase was increased. Roentgen examination of the skeleton revealed moderate osteoporosis.

Treatment consisted of a diet low in fat, high in protein and containing as many as fourteen bananas daily. Under this therapeutic regimen the patient improved markedly. Five months after the inauguration of treatment and one year after the beginning of the illness his condition was "almost normal." A dextrose tolerance test performed at this time (weight, 27 Kg.; dextrose, 52 Gm.) showed a more normal type of blood sugar curve and no glycosuria. Gastric hydrochloric acid reappeared in moderate quantity. A second metabolic study of the fat and nitrogen balance performed during the ninth month of treatment and the sixteenth month of the illness showed results not significantly different from those of the first investigation.

The diagnosis of acute pancreatogenous fatty diarrhea was based on the presence of steatorrhea and azotorrhea, the altered response to the dextrose tolerance test and the elevation of urinary diastase. Differential diagnosis involved the exclusion of the Gee-Herter-Heubner celiac syndrome, abdominal tuberculosis and nontropical sprue. Each of these was ruled out to the satisfaction of the author. The prognosis for this child must be guarded, because of the notorious tendency to recurrence characteristic of this type of diarrhea.

MCCUNE, New York.

HEMATURIA DURING TREATMENT WITH INSULIN. A. J. JOOSTEN, Nederl. tijdschr. v. geneesk. **77**:3779 (Aug. 19) 1933.

Severe hematuria occurred in two diabetic boys, aged 13 and 16 years, one day after admission to the hospital, after an intensive course of insulin therapy had been begun for the existing precoma. The prognosis is favorable.

VAN CREVELD, Amsterdam, the Netherlands.

PROPHYLAXIS AND TREATMENT OF DISEASES WITH ULTRAVIOLET RAYS. E. GORTER, Nederl. tijdschr. v. geneesk. **77**:4781 (Oct. 21) 1933.

Only in rickets are the factors determining the favorable action of ultraviolet rays completely known. It has been shown that ergosterol deposited in the skin is transformed into vitamin D by the action of ultraviolet rays. Only rays having a wavelength of from 2,950 to 3,100 angstrom units are active. The minimum energy required to cure rickets is 0.1 calorie. The minimum amount of ergosterol necessary to cure rickets is 0.001 mg. per kilogram of body weight.

It is probable that many other diseases can be improved by the action of ultraviolet rays, but present knowlege of the wavelength and the energy required to produce an effect is scanty. The hypothesis that ultraviolet rays produce antibodies in the skin has had many defenders.

VAN CREVELD, Amsterdam, the Netherlands.

TREATMENT OF COLITIS ULCEROSA WITH BLOOD TRANSFUSIONS. L. A. HULST and H. A. P. HARTOG, Nederl. tijdschr. v. geneesk. **78**:1849 (April 28) 1934.

Four cases of colitis ulcerosa in adults who were treated with blood transfusions are reviewed. In two cases improvement followed promptly. In the other two improvement occurred only after repeated transfusions. If improvement does not follow, it is desirable to repeat transfusions, using blood from another donor. The favorable effect cannot be explained.

VAN CREVELD, Amsterdam, The Netherlands.

LIPOGRANULOMATOSIS. S. M. KROPVELD, Nederl. tijdschr. v. geneesk. **78**:1860 (April 28) 1934.

A rare case of fat necrosis with a strange microscopic aspect, characterized by foci of lymphocytes, is described.

VAN CREVELD, Amsterdam, The Netherlands.

HETEROPHILIC ANTIBODIES IN GLANDULAR FEVER. L. MEYLER and R. J. SIEMELINK, Nederl. tijdschr. v. geneesk. **78**:1952 (May 5) 1934.

Heterophilic antibodies, demonstrable in the form of sheep cell agglutinins, were found in rather high concentrations in six cases of infectious mononucleosis. Four of the patients were children. Recently, this phenomenon was described by the American authors Paul and Bunnell. It cannot be doubted that it is a valuable diagnostic aid in differentiating infectious mononucleosis from other diseases.

The authors used this test in 400 hospitalized patients with miscellaneous conditions. They did not observe an appreciable increase of heterophilic agglutinins, except in one case of subacute myelogenous leukemia and one case of jaundice caused by gallstones.

VAN CREVELD, Amsterdam, The Netherlands.

Nervous Diseases

THE DIAGNOSIS AND LOCALIZATION OF TUMORS OF THE SPINAL CORD BY MEANS OF MEASUREMENTS MADE ON THE X-RAY FILMS OF THE VERTEBRAE, AND THE CORRELATION OF CLINICAL AND X-RAY FINDINGS. CHARLES A. ELSBERG and CORNELIUS G. DYKE, Bull. Neurol. Inst., New York **3**:359 (March) 1934.

Elsberg and Dyke emphasize the value of measurement of the width of the spinal canal as an aid in the diagnosis of tumors of the spinal cord. They determined the normal variation in the distance between the pedicles and found distinct changes in the space in cases of tumors. In tumors of the spinal cord there is often an increase in the size of the vertebral canal at the level of the growth.

This enlargement was found in 42 per cent of the sixty-seven cases studied. In extramedullary tumors increase in the size of the canal was found in 18 per cent of the cases studied, while in extradural tumors the enlargement occurred in 74 per cent. Also, at the level of the tumor the inner borders of the pedicles of the vertebrae were often flat and sometimes concave.

BEVERLY, Chicago.

THE NITRITE OF AMYL TEST FOR THE DIFFERENTIATION OF TUMORS OF THE BRAIN FROM VASCULAR AND CHRONIC INFLAMMATORY LESIONS: A PRELIMINARY REPORT. CLARENCE C. HARE, Bull. Neurol. Inst., New York **3**:513 (March) 1934.

The author studied the effect of the inhalation of amyl nitrite on changes in pressure of the cerebrospinal fluid in various lesions of the brain. The drug normally produces dilatation of the intracranial blood vessels, with consequent forcing of the cerebrospinal fluid from the cranial cavity into the subarachnoid space of the vertebral column. In vascular or inflammatory disease the effect of the drug is limited, as full dilatation of the intracranial blood vessels does not occur. There is, therefore, a lessened increase in the cerebrospinal fluid pressure. In tumors of the brain, on the other hand, there is little, if any, interference with the dilatation of the intracranial blood vessels, and the intracranial pressure is increased by the inhalation of amyl nitrite. Occasionally, the early symptoms of tumor are not due to the neoplasm but are the result of interference with the blood supply to part of the brain, caused by occlusion of a large blood vessel. In these cases, therefore, this test would be of no value in the differential diagnosis.

BEVERLY, Chicago.

CRIMINALITY AND DELINQUENCY IN TWINS. AARON J. ROSANOFF, LEVA M. HANDY and ISABEL A. ROSANOFF, J. Crim. Law & Criminol. **24**:923 (Jan.-Feb.) 1934.

Records were taken from 1,008 pairs of twins of whom one or both were affected by mental disorder and from 313 pairs of normal twins. From these a study has been made of criminality, juvenile delinquency and behavior difficulties, which shows that causative factors of mental and behavior difficulties are pregerminal, germinal, embryonic, fetal, natal or postnatal, and that they may be simple, multiple (or variable) or complex. Comparisons are made with the studies of Johannes Lange in Germany and of Legras in Holland. The findings show that criminality is significantly more common in the male than in the female sex, though this contrast is less marked in the group showing juvenile delinquency and almost nonexistent in the group with behavior difficulties in childhood. Monozygotic twins are more closely alike than are any other two persons who could be selected, but "identical twins" are nonexistent. Injury to the head may produce a change in a person's character that may establish persistent criminal tendencies which previously did not exist. This study indicates that in two thirds of the cases of adult criminality in monozygotic twins if one is criminal both are criminal. In the remaining one third of the cases, in which only one of each pair of twins is criminal, five possible explanations for the development of the criminal tendencies are cited. In the juvenile delinquency group, of 16 pairs of male dizygotic twins only one was affected in 5 instances, and of 9 pairs of female dizygotic twins both were affected in all cases.

SELLING, Joliet, Ill. [ARCH. NEUROL. & PSYCHIAT.]

CALCIUM IN EPILEPSY. G. M. GRIFFITHS, J. Neurol. & Psychopath. **15**:29 (July) 1934.

While the serum calcium of persons with epilepsy falls within normal limits, there were wide variations in the 433 estimations made on a group of 48 persons in a colony for patients with this disease. Generally the average of values before

a seizure is greater than that after the fit. The highest range was obtained during a run of fits, while the lowest were found after a run. As regards phosphorus, the values agree with the findings for calcium, the lower value for phosphorus before fits corresponding to the higher values for calcium, and vice versa. When cases of fits by day are contrasted with those of fits by night, the averages show that the behavior of the serum calcium in relation to the attacks varies inversely in the two groups.

Eight patients with low values for calcium were given calcium gluconate and cod liver oil and a pint of milk daily in addition to their regular diet for a period of four months. Five showed an increased calcium level, though with some fluctuation. Two showed an increase in the incidence of the fits. In two there was no change, and in the other there was some degree of improvement. In two of these cases the seizures increased on the cessation of calcium treatment. In one case the improvement resulting from the calcium treatment was marked.

JAHR, Omaha.

COLLOID CYST OF THE THIRD VENTRICLE ASSOCIATED WITH CONGENITAL CYSTIC KIDNEYS. E. WYN JONES and DOUGLAS H. COLLINS, J. Neurol. & Psychopath. **15**:53 (July) 1934.

Two days before admission to the hospital a 16 year old boy received a slight blow on the head. He complained of severe headache, nausea and vomiting. The following day he became stuporous and gradually sank into coma. On examination his attitude was that of cerebral irritation. The pulse rate was 60, the respiratory rate 24 and the temperature 97 F. Neurologic examination was inadequate, though there were found bilateral papilledema, dilatation of the pupils, with sluggish reaction to light, and paresis of both internal recti. The knee and ankle jerks were sluggish, and the plantar responses were bilaterally extensor. There was hyperalgesia bilaterally. There was urinary incontinence, and the urine contained a large amount of albumin. The spinal fluid was under increased pressure; it was clear, with 28 cells (mostly lymphocytes) per cubic centimeter. The boy's condition became rapidly worse, and he died three hours after admission. Postmortem observations were: a large edematous brain, with both lateral ventricles dilated and distended with clear fluid. Almost filling the third ventricle and attached to the choroid plexus of the velum interpositum was a spherical thin-walled cyst 1.5 cm. in diameter.

Both kidneys showed polycystic changes, the cysts varying in size from that of a pinhead to 44 mm. across. There were caseous foci in the upper lobe of the left lung and the lower lobes of both lungs.

JAHR, Omaha.

POSTERIOR BULBAR TUMOR IN A CHILD WITH BILATERAL SIXTH CRANIAL NERVE PARALYSIS; EFFECTIVENESS OF INTRAVENOUS HYPERTONIC SALINE INJECTIONS. J. CHAPTAL and H. VIALLEFONT, Bull. Soc. de pédiat. de Paris **31**:41 (Jan.) 1933.

A boy, 6 years old, had the cardinal symptoms of tumor of the brain. The neurologic signs and symptoms pointed to localization of the lesion in the floor of the fourth ventricle. At intervals he showed evidence of markedly increased intracranial pressure. This was readily relieved by the intravenous injection of 20 cc. of a 20 per cent sodium chloride solution. Operation was advised, but the parents refused to permit surgical intervention. The child became steadily worse after his removal from the hospital and was on the point of death when last heard of.

BENJAMIN, Montreal, Canada.

TUMOR OF THE VALVE OF VIEUSSENS. J. EUZIÈRE, E. LEENHARDT, H. VIALLEFONT and J. CHAPTAL, Bull. Soc. de pédiat. de Paris **31**:47 (Jan.) 1933.

A boy, 12 years of age, began to have repeated and persistent vomiting. After some observation a number of physicians agreed that he was suffering from

appendicitis and recommended appendectomy. The day before the date set for the operation high fever developed, and the operation was postponed. Signs and symptoms which pointed definitely to the diagnosis of tumor of the brain then began to develop. He died suddenly. Necropsy revealed a glioma in the midline at the level of the valve of Vieussens encroaching on the canal of Sylvius and the superior part of the posterior wall of the fourth ventricle; anterior to the third ventricle, in front of the chiasma, was a cyst which contained about 500 cc. of apparently normal spinal fluid. Two doses of roentgen rays of high voltage had been administered without any beneficial result. The onset with marked digestive disturbance which led to a mistaken diagnosis of appendicitis is emphasized, as well as the repeated tonic seizures and the urinary incontinence in the presence of a tumor of the posterior fossa.

BENJAMIN, Montreal, Canada.

THE NERVOUS CHILD. M. PÉHU, Rev. méd. sociale de l'enf. **1**:402 (Nov.-Dec.) 1933.

Péhu considers that in the vast majority of cases the nervous child who cannot fix his attention, refuses to eat, sleeps poorly or shows other manifestations of an unbalanced nervous system is not born so but that these tendencies are allowed to develop through faulty education and environment. He has a word of scorn for parents who boast of their high-strung child and who shower on an only child every form of concentrated attention. A firm, just supervision with the development of a regular routine often changes an unstable child into one who is well balanced and happy. Strict governesses who keep children too long at work may cause trouble as severe as that caused by careless nurse-maids who excite and frighten their charges. Parents and particularly grandparents must agree in their treatment of children, for a child who is battered between extremely lenient and extremely harsh treatment is confused and cannot find himself.

LESLIE, Evanston, Ill.

CLINICAL AND ANATOMICOPATHOLOGIC OBSERVATIONS IN A CASE OF ANGIORETICULOMA OF THE BRAIN IN AN INFANT. A. PICCIOLI and L. MENCARELLI, Pediatria **42**:569 (June 1) 1934.

The authors report a case of cerebral angioma. A detailed presentation of the anatomicopathologic picture, together with a description of the clinical manifestations, is given. The case is of great interest, particularly because of the rarity of this condition in infants and because it reminds one of the necessity of being prepared to recognize clinically even conditions which ordinarily are unsuspected.

A boy, 7 years of age, presented from the beginning evidence of motor excitability, with occasional clonic movements of the right arm. The reactions of Pandy, Nonne, Appelt and of Boveri were weakly positive Bacteriologic examination of the cerebrospinal fluid failed to reveal the presence of Koch's bacillus or any other micro-organism, and there was no flocculence.

A review of the literature on the subject is given.

SIGNORELLI, New Orleans.

MODIFICATION OF THE TENSION OF THE CEREBROSPINAL FLUID BY MEANS OF HYPERTONIC SALINE SOLUTIONS OF VARYING CONCENTRATIONS. S. STEFANINI, Riv. di clin. pediat. **32**:425 (April) 1934.

Stefanini reports observations on eighteen patients with increased pressure of the cerebrospinal fluid. The intravenous injection of 10 per cent sodium sulphate solution resulted in rapid diminution of the spinal fluid pressure. Enemas of 5 or 10 per cent sodium sulphate resulted in similar reduction of the spinal fluid

pressure. In each case the pressure remained lowered for twenty-four hours. Daily use of sodium sulphate enemas resulted in most cases in stabilization of the spinal fluid pressure as effectively as the not always practicable repeated lumbar puncture.

The use of atropine to reduce the spinal fluid pressure was in general unsatisfactory, as the results were uncertain.

HIGGINS, Boston.

INTRODUCTION TO THE PSYCHIATRY OF INFANCY. J. P. VILA, Arch. de med. inf. **2**:184 (April) 1933.

This article is the last of a series on the psychiatry of infancy and contains valuable statistics relating to the mental growth of Cuban children.

SANFORD, Chicago.

THE TEACHING OF PSYCHOANALYSIS. EURYALO CANABRANA, Arch. de pediat., Rio de Janeiro **6**:771 (May) 1934.

The author discusses some of the problems and aims of the teacher of psychoanalysis.

SANFORD, Chicago.

INFANTILE PSYCHOSES. A. VALLEJO NÁJERA, Paidoterapia **12**:1211 (April) 1934.

In a study of infantile psychoses at the San José Psychiatric Sanatorium the author describes thirteen of the forty-five patients. The majority of the patients described have various types of schizophrenia.

The group of infantile psychoses must be reduced to a series of endogenous syndromes, principally, schizophrenia, imbecility, epilepsy and postencephalitis. Several authors have pointed out the rarity of mental disease in children, and Willinger recently confirmed this in Germany on observing only three cases of infantile psychosis in 10,000 school children examined.

Heller's infantile insanity is characteristic in that there is rapid cerebral involution which leads in a few months to profound insanity, the intelligence being completely destroyed.

In the author's series of forty-five patients only three had no family history of mental disturbance. The cause of the acute or chronic onset is unknown. In the acute form the symptoms are accentuated anxiety, hallucinations, dulling of the sense of touch and a typical loss of mental power. In the chronic form the child ceases to be able to learn; other patients know facts but cannot express them. The forms of schizophrenia occurring in puberty resemble the form in the adult. They may be acute or chronic.

HERRON, Spokane, Wash.

HEINE-MEDIN DISEASE. DANERI, Rev. chilena de pediat. **4**:449 (Oct.) 1933.

Daneri recommends the use of convalescent serum in the treatment of Heine-Medin disease. It is most effective if used early and in the preparalytic stage. The author reports good results in the dangerous ascending bulbar type. Little effect is seen if the injection is delayed too long. The serum may be given intramuscularly or intraspinally. From 10 to 20 cc. is given daily, if given intramuscularly, and 10 cc. daily for several days, if given intraspinally.

SCHLUTZ, Chicago.

INVESTIGATIONS ON THE EFFECT OF PERORAL PHOSPHATE ON TETANY. K. SCHINDLING, Monatschr. f. Kinderh. **59**:245, 1934.

As rickets is generally considered associated with a diminution in the inorganic serum phosphate, Schindling studied the effects on the development of tetany of a

patented phosphate-containing drug given subcutaneously. There is unquestionably an increase in the phosphate content of the blood following injection. The height of the increase is dependent on the amount of phosphate injected, the size of the child and a third factor which probably depends on whether florid rickets is present. The hypothetic danger in giving phosphate lies in its depleting the body of calcium. However, checking up on the electrical reactions, Schindling found that electrical excitability was increased only when rachitic children received the phosphate in doses of 0.5 Gm. per kilogram of body weight. Nonrachitic children were unaffected. He concludes that this drug can be used at all times in children not suffering from rickets.

GERSTLEY, Chicago.

HEREDITY IN SYRINGOMYELIA. B. N. MANKOWSKY and L. I. CZERNI, Ztschr. f. d. ges. Neurol. u. Psychiat. **143**:701 (Jan.) 1933.

According to the theory of Bielschowsky and Henneberg, syringomyelia is spongioblastosis which is dependent on the failure of the medullary canal to close properly. Henneberg also distinguished two types of failure to close: arraphia, due to the absence of the normal raphes, and dysraphia, due to inhibition in the approximation of the raphes. Spina bifida, diplomyelia and rachischisis belong to the first group; syringomyelia, hydromyelia, myelocystocele, spinal gliosis and glioma formation belong to the second group.

Reports of familial syringomyelia are few. Probaschenski (1899) reported cases in a father and two daughters; Nalbandow (1899) observed cases in a mother and son. Clarke and Growes (1909) reported two cases in one family. Other cases have been reported in a father and son, in brothers and in a father and two sons. Bremer (1926) studied all the members, both healthy and diseased, in ten families with syringomyelia. In addition to one family with two brothers suffering from the disease, he found a number of anomalies among the "healthy" members, such as chicken breast, kyphoscoliosis, cyanosis and coldness of the distal parts of the extremities, enuresis, anomalies of the growth of hair, poor teeth and syndactylism. Shortly after this Kino described cases of syringomyelia in a father, aged 66, and his three daughters, the localization of the process being the same in all the cases. Kino found also that five generations of this family had suffered from angiospastic phenomena in the fingers.

Mankowsky and Czerni report the cases of two brothers and of two sisters with syringomyelia, the two groups being in two different families. They believe that heredity is more common than is reported in this disease, and that these cases indicate that syringomyelia is a true heredodegeneration.

ALPERS, Philadelpha. [ARCH. NEUROL. & PSYCHIAT.]

CHANGES IN EXCRETION OF CREATINE AND CREATININE IN PROGRESSIVE MUSCULAR ATROPHY AFTER ADMINISTRATION OF GLYCOCOLL. A. G. SCHOO and J. BOER, Nederl. tijdschr. v. geneesk **78**:32 (Jan. 6) 1934.

An investigation was made of the excretion of creatine and creatinine in two children suffering from progressive muscular atrophy. It appeared that the amount of creatine excreted in these cases after the administration of glycine was considerably larger than in six healthy children examined. The administration of glycine during six weeks influenced the excretion of creatine in the sick children to such a degree that it came within the bounds for that in normal children. After discontinuing the administration of glycine the quantity of excreted creatine again became much larger in the sick children than in normal children. It is pointed out that this alteration in the amount of creatine excreted probably indicates an altered metabolic process in the muscles, occasioned by the administration of glycine. However, the authors could note no perceptible clinical improvement in these cases.

VAN CREVELD, Amsterdam, The Netherlands.

Diseases of the Eye

CONGENITAL PARALYSIS OF LATERAL MOVEMENTS OF THE EYES WITH UNILATERAL FACIAL PARALYSIS. L. DUPUY-DUTEMPTS, Bull. Soc. d'opht. de Paris, July 1934, p. 365.

At the age of 8 years the oldest of three children showed the rare condition of paralysis of lateral gaze (the two younger children had no anomalies). With this condition and complete paralysis of the right facial nerve the child presented a strange physiognomy.

In spite of the child's intelligence and normal fundi the visual acuity could not be enhanced from 0.3 for the right eye and 0.6 for the left. The eyes were directed parallel, without apparent strabismus. The left facial nerve was intact. The movements upward and downward were excellent, and convergence was normal.

The initial observation of this type of case was made by Foville in 1858. The work of Laborde, Duval and Bernheimer demonstrated that the nucleus of the sixth cranial nerve is the common motor center for laterality of gaze. The proximity of the facial and abducens nerves may account for the involvement of both nerves. In cases reported by Harlan (1875), Möbius (1888), Scharpinger (1889), Jacquean (1903), Fryer (1903) and Bielschowsky in the Graefe-Saemisch handbook there was bilateral facial paralysis. In spite of the lack of anatomic investigation it is reasonable to suppose that the lesion is one of congenital damage to the cells of the nucleus of the sixth cranial nerve.

L. L. MAYER, Chicago. [ARCH. OPHTH.]

THE RELATION BETWEEN MICROPHTHALMUS WITH CYST OF THE LOWER LID AND GENERAL MALFORMATIONS. E. VON HIPPEL, Arch. f. Ophth. **132**:256 (April) 1934.

Von Hippel had the opportunity to examine four specimens showing extensive general malformations which were the property of the Pathological Institute of the University of Göttingen. In all four cases both orbits with their contents could be studied anatomically. The bulbi were all microphthalmic and communicated with typical cysts of the lower lid. The fact that in these four cases and in others reported in the literature large congenital cysts were found in the brain, kidney, pancreas and liver made the author think of a relation between microphthalmus and the symptom complex of Lindau. Besides, he found in one of the four cases a capillary angioma in the retina. Other interesting findings in the microphthalmic eyes were extensive cystic degeneration of the retina and entropion iridis.

P. C. KRONFELD, Peiping, China. [ARCH. OPHTH.]

TREPHINING AFTER ELLIOT IN CONGENITAL HYDROPHTHALMOS FOLLOWED BY PROLAPSE OF THE RETINA INTO THE ANTERIOR CHAMBER: REPORT OF A CASE. O. KARASEK, Klin. Monatsbl. f. Augenh. **92**:389 (March) 1934

A girl, aged 7, had bilateral congenital hydrophthalmos. The corneal diameters were 11 mm. vertical by 11.5 mm. horizontal in the right eye, and 13.5 mm. vertical by 14 mm. horizontal in the left. Scleral trephining after Elliot, done by A. Elschnig, was uneventful in the right eye, but was followed by total detachment of the retina in the left. On the second day after the operation, when the cornea had cleared, further changes could be noticed. The lateral pillar of the coloboma was pushed toward the cornea by a fold of the retina. The lens, examined with the slit lamp later on, was subluxated nasalward and downward; it was perfectly clear, so that the detached retina could be observed behind it. The prolapsed portion of the retina had retracted spontaneously two months later, but the retina remained detached; no tear was found. The vision was reduced to uncertain perception of light; the tension remained low.

The cause of the prolapse and detachment of the retina was the sudden escape of the aqueous humor and the liquefied vitreous and, probably, partial luxation of

the lens prior to the operation; distinct iridodonesis had been noted on admission to the hospital. The detachment of the retina occurred immediately after the escape of the intra-ocular fluid, in Karasek's opinion, but not as a consequence of a detachment of the choroid and retina.

K. L. Stoll, Cincinnati. [Arch. Ophth.]

Reaction of Pupils to Light and Allergy. B. S. Beilin, Vrach. delo **17**:379, 1934.

Beilin calls attention to the fact that not only diminution or absence of reaction of the pupils to light is of importance, but also, on the contrary, that a lively reaction to light may have a definite pathologic significance. He noted the latter condition in patients suffering from certain allergic states, for the most part, in those who had urticaria or who had a history of such an eruption. Characteristic features of this "liveliness" of the pupil reaction are the greater amplitude as well as the quicker rate of the latter. There is no question of raising the theshold of excitability. The occurrence of this type of pupillar reaction in allergic patients is to be explained by the fact that under the influence of special substances or owing to the peculiar sensibility of the vasomotors, the organism of an allergic person becomes sensitized to a series of physical, chemical or even psychical factors, and the vivid pupillary reaction to light is only a particular manifestation of this increased excitability.

Yampolsky, Atlanta, Ga.

Diseases of the Ear, Nose and Throat

Nasopharyngeal Fibroma. William Brewster Allan, Arch. Otolaryng. **19**:216 (Feb.) 1934.

Nasopharyngeal fibroma is a rare vascular tumor found most often in adolescent boys. It is composed chiefly of connective tissue and has many blood vessels which are almost devoid of a contractile coat. Its origin is connective tissue in the vault of the pharynx and the postnasal space. There is evidence of retrogression in early adult life, which may be due to a change in blood supply brought about by the ossification of the cartilaginous plate between the sphenoid and the occipital bone. The growth occurs mostly in males and may undergo sarcomatous and carcinomatous changes.

Surgical removal has led to facial deformity and loss of life from hemorrhage and shock. The treatment is implantation of radon seeds into the base of the tumor.

Greenwood, Chicago.

Dentigerous Cysts of the Antrum: Report of Two Cases. Andrew A. Love, Arch. Otolaryng. **19**:348 (March) 1934.

Love states that the essential etiology of this condition is not known but is probably retention of fluid in the stellate reticulum of the follicle of the tooth that is situated between the cuticular dentin and the crown. The fluid distends the follicle into a cyst lined with adamantine epithelium. The majority of such cysts develop from unerupted permanent teeth and usually appear between 10 and 30 years of age. Love commends the work of Malassez, who believed that these cysts develop from paradental rests. He remarks that Cohnheim's theory of tumor formation, according to which there must be a matrix of embryonal cells, falls down here, for in this condition there is a displaced matrix of embryonal cells which may be typical and carry out their life function in an abnormal position. Although composed of misplaced epithelium, they do not form malignant growths. He presents a good differential diagnosis, referring to radicular cysts, and concludes that the most successful treatment is complete removal by a radical operation on the antrum.

Greenwood, Chicago.

ETIOLOGY AND PATHOLOGY OF PARALYSIS OF THE ABDUCENS NERVE ASSOCIATED WITH SINUS THROMBOPHLEBITIS. SAMUEL D. GREENFIELD, Arch. Otolaryng. **19**:336 (March) 1934.

Greenfield cites work done by Gradenigo, Perkins, Eagleton, Kopetzky, Almour and others on abducens palsy resulting from a pathologic condition of the petrous tip. He refers to the anatomy of the abducens and in describing its course demonstrates its close relation to the inferior petrosal sinus in Dorello's canal. He points out that the two sixth cranial nerves are from 5 to 6 mm. apart for a distance of 15 mm.

Further, he remarks on the close contact of the inferior and superior petrosal sinuses on entering the cavernous sinus and then proceeds to state how much thrombosis of one or both unilateral petrosal sinuses there may be. When there are phlebitis and periphlebitis, there is much greater edema than with simple venous stasis of the sinuses, with resultant greater likelihood of unilateral and bilateral abducens palsy. He cites a case in point of a complete obliterative thrombus extending from the torcular Herophili to the subclavicular area, with bilateral sixth nerve paralysis; there was no involvement of the petrous tip. An operation was performed, and recovery was complete.

GREENWOOD, Chicago.

IS THE REMOVAL OF TONSILS AND ADENOIDS CONTRAINDICATED IN YOUNG CHILDREN? MARCEL OMBREDANNE, Presse méd. **42**:799 (May 16) 1934.

Ombredanne attacks the three arguments usually offered against removal of tonsils and adenoids before the sixth or seventh year, namely, that hypertrophied tonsils and adenoids are simply the manifestation of a general defective state; that the operation is likely to be attended by shock or fever, and that the growth is likely to return and that the lymphoid tissue plays a defensive rôle against infections. All three arguments are fallacious, Ombredanne states; he believes that the infected tissue is a veritable culture tube for infectious organisms, and that proper removal is as safe in young children as in older ones and no more likely to be followed by return of the growth. The principal reasons for early removal are: (1) to insure free ventilation so necessary to health in general and to proper growth of the chest in particular, (2) to avert the many infections, e. g., otitis, bronchopneumonia and numerous intestinal, renal and glandular disturbances, the chief portal of entry of which is by way of the tonsils and adenoids. If possible, it is best to avoid the operation in the first two years, but after that time the child's condition is much the same as in the few years that follow, and while the operation is a little more difficult the consequences are not as much to be feared as has been believed.

BIEKER, St. Petersburg, Fla.

Diseases of the Skin

HEREDITARY ECTODERMAL DYSPLASIA OF THE ANHIDROTIC TYPE, WITH CASE REPORT. J. MARK HIEBERT and JOSEPH GARLAND, New England J. Med. **210**:784 (April 12) 1934.

This condition occurred in a boy aged 5 years and 10 months. A paternal grand-uncle is said to have been endentulous until the age of 5 years, after which a normal set of permanent teeth developed. The patient was normally delivered at term, weighing 7 pounds. He held his head up at the age of 4 months, sat alone at the age of 8 months and walked at the age of 17 months. The first tooth was cut at the age of 11 months, and at the time of writing he had two canines in the mandible and one incisor, two canines and two molars in the maxilla; all the teeth were tusk-shaped and widely spaced. In spite of this imperfect dentition he masticated his food in a fairly effective manner. The patient never perspires, even in the hottest weather. The hair has always been sparse and is exceedingly fine, with a tendency to break; there are scattered areas of alopecia. The palms

and soles are always dry and scaly. The voice has always been hoarse, and he has frequent attacks of complete aphonia. The height is 42½ inches (107.9 cm.); the weight, 42 pounds (19.1 Kg.). The eyebrows are absent, although a few scattered eyelashes are present.

Laboratory tests showed normal urine and blood. The tuberculin and Hinton tests gave negative results. The basal metabolic rate was average, plus 8 per cent. The blood sugar during fasting was 97 mg. per hundred cubic centimeters; the cholesterol was 154 mg., the serum calcium, 11.45 mg., and the serum phosphorus, 4.48 mg. The temperature of the skin was taken as described by Talbot. The following results were obtained.

	Patient, C.	Standard, C.
Average temperature of face	35.2	32.2
Average temperature of trunk	37.1	35.5
Average temperature of extremities	35.4	33.0
Average rectal temperature	37.8	

The temperatures of the skin of the patient, therefore, equalled those of normal children with rectal temperatures of 40 C., or 104.5 F. A specimen of skin taken from the back between the shoulder blades was examined and showed no hair follicles, sweat glands or sebaceous glands.

Roentgenograms revealed four unerupted teeth in the mandible and two in the maxilla.

GENGENBACH, Denver.

HERPES ZOSTER IN AN INFANT AGED TWO YEARS. L. BABONNEIX, L. PERIN and J. DAVID, Bull. Soc. franç. de dermat. et syph. **40**:1753 (Dec.) 1933.

Because of the great rarity of such an occurrence at so early an age, a typical case of herpes zoster occurring on the left side of the thorax in an infant aged 2½ years is reported.

GANDY, Houston, Texas. [ARCH. DERMAT. & SYPH.]

BROMODERMA IN A SUCKLING. SPILLMANN, WATRIN, WEIS and ROSENTAL, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Nancy) **41**:2 (Jan.) 1934.

A case of bromoderma in a nursling 7 months old is reported. The eruption was generalized but was most profuse on the face. The lesions were of the vegetating, papulotuberculous type, some measuring 6 cm. in diameter. There were no subjective symptoms. The infant had been erroneously treated for syphilis for several weeks. The mother was taking bromides for epilepsy, and chemical analysis of her breast milk and urine disclosed bromide. Histologic study showed the usual picture of a vegetating bromoderma.

GANDY, Houston, Texas. [ARCH. DERMAT. & SYPH.]

SODIUM HYPOSULPHITE IN THE TREATMENT OF SCABIES AND VARIOUS CUTANEOUS CONDITIONS. RAVAUT and MAHIEU, Bull. Soc. franç. de dermat. et syph. **41**:135 (Jan.) 1934.

Addition of an acid to a solution of sodium thiosulphate results in the precipitation of fine grains of colloidal sulphur. This fact is utilized by Ravaut and Mahieu in a new method of treatment for scabies. After a bath of soap and water the patient rubs on a 40 per cent solution of sodium thiosulphate and then applies a 4 per cent solution of hydrochloric acid. A deposit of sulphur forms on the skin. It is allowed to dry, and the procedure is repeated. The patient then dresses and goes about his occupation. The same operation is repeated the following day. Usually only two treatments are necessary, although the procedure may be repeated for several days in succession. It is a rapid, harmless, convenient and cheap method of treatment. Ravaut and Mahieu tested it on fifty-two patients with scabies (microscopically proved) which had been present from six days to six

months; in fifteen of these patients other methods of treatment had failed, but perfect results followed the application of the new therapy. The authors found this procedure valuable also for other cutaneous conditions for which sulphur is indicated.

GANDY, Houston, Texas. [ARCH. DERMAT. & SYPH.]

THALLIUM ACETATE IN THE TREATMENT OF SCURF AND TRICOPHYTIC DISEASE. P. TIMPANO and G. CASTORINA, Pediatria **42**:485 (May 1) 1934.

The authors call attention to the frequency of scurf and trichophytic disease in children and point to their obstinacy to curative measures originally employed without depilation.

They present a report of the study of forty-eight children suffering from this disease, thirty of whom were treated with thallium acetate alone and eighteen with half doses of thallium in combination with the roentgen rays, half the usual exposure being utilized. Their results lead them to the conclusion that thallium alone gave more complete, constant and permanent relief than the use of thallium in combination with the roentgen rays.

SIGNORELLI, New Orleans.

Miscellaneous

DENTISTRY'S PLACE IN CHILD WELFARE. G. S. MILLBERRY, J. Am. Dent. A. **21**:1176 (July) 1934.

Dr. Millberry heartily advocates the inclusion of dental health service in all programs of child welfare and cites the lack of this point of view in existing plans as responsible in a large measure for the inadequate concept in the minds of both professional and lay persons. He mentions also the extremely inadequate background furnished by the medical curriculum. He suggests the division of the subject into the following age groups: (1) prenatal, (2) from birth to 3 years, (3) from 3 to 6 years, (4) from 6 to 12 years, (5) from 12 to 18 years and (6) from 18 to 24 years. He also mentions the importance of adequate preparation on the part of the medical and dental professions to permit intelligent cooperation in these programs.

NOYES, Chicago.

IS AN OPERATIVE PREVENTIVE MEASURE PRACTICAL? THADDEUS P. HYATT, J. Am. Dent. A. **21**:1209 (July) 1934.

Hyatt forcefully presents evidence secured from the study of caries on the various tooth surfaces of 408,096 teeth from the mouths of 12,753 persons and contends that the cause of dental caries lies in the action of acidogenic and proteolytic bacteria on carbohydrate detritus which accumulates on a tooth surface. His statistics reveal a striking predominance of caries on the tooth surfaces which contain pits and fissures, as contrasted with smooth surfaces of the teeth. Reasoning from these data, he reiterates the importance of a procedure by which these pits and fissures are cleaned and the place of lodgment of bacteria and food material obliterated by filling with a suitable material. This he has called prophylactic odontotomy. The procedure is efficacious, he believes, because it "prevents the accumulation of carbohydrates in an uncleanable place. . . . prevents the localization of undisturbable bacteria at a definite point" and "prevents the small hole's remaining a protected laboratory for the production of those acids which break down the substance of the tooth."

NOYES, Chicago.

TRENDS IN PEDIATRICS. JOHN RUHRÄH, J. Pediat. **4**:715 (June) 1934.

This is the address delivered by the outgoing president of the American Academy of Pediatrics. The advance of pediatrics is reviewed, and it is shown how progress in pediatrics has always been shaped by the character of the age.

To consciously direct the trends in pediatrics is more desirable than to let chance events determine their course. It seems desirable in infant welfare work to direct attention to ways of producing better babies in addition to ways of preventing sickness and maintaining life in those already born. The importance of teaching art as well as science to practioners of pediatrics is discussed. Ruhräh also suggests the need of better methods for sifting out the best of modern knowledge in pediatric teaching. The aims and problems of the academy are discussed.

LEMASTER, Evanston, Ill.

INFANT MORTALITY STUDIES IN WEST VIRGINIA. GEORGE M. LYON, West Virginia M. J. **30**:289 (July) 1934.

This article is a splendid summary of some of the surveys made for and presented at the West Virginia White House Conference on Child Health and Protection in 1933. The study presents a cross-section of the work in the state as a whole; it is extensive and is illustrated by many maps and graphs. It does not lend itself to abstraction.

SHAWKEY, Charleston, W. Va.

LIGHT TREATMENT—AN HISTORICAL REVIEW. R. KING BROWN, Brit. J. Phys. Med. **8**:169 (March) 1934.

This issue of the journal is devoted to "Light Treatment in Present-Day Practice." The editorial presents a historical review of the use of natural sunlight and artificial light therapy. There is an excellent conservative summary of the results achieved with this form of therapy.

HARTMAN, Cleveland.

HOW TO CONDUCT A BABY SHOW. A. M. GEDDES, South African M. J. **8**:251 (April 14) 1934.

In grading infants at a baby show Geddes divides the entrants into groups, the younger infants being divided into classes of those of 3 months, and the older ones into classes of those aged 6 months. Different criteria are used for the different age groups. For infants from 7 to 12 months of age he grades on the following basis: weight, 20; tone, 20; skin, 15; color, 10; hair, 10; muscular development, 10; teeth, 10; fontanel, 5.

GONCE, Madison, Wis.

INFANT WELFARE STATIONS IN JAVA. D. P. R. KEIZER, Nourrisson **22**:79 (March) 1934.

This is a report on the work accomplished among the infants of Java. Europeans, Javanese and Chinese are all encouraged to come to the infant welfare stations. In addition to the problems of hygiene and infant feeding are those of infections, both the ubiquitous and tropical varieties. Dysenteries, beriberi, xerophthalmia and rickets are all encountered, as well as diphtheria, tuberculosis, congenital syphilis, malaria and infantile paralysis. The rarities are pyloric stenosis, spasmophilia, congenital heart disease and mongolian idiocy. All other pediatric diseases and infections are encountered as frequently as in the more temperate climates. Bronchopneumonia is a frequent finding in those dying from alimentary disturbances. When native mothers nurse their infants exclusively more than five or six months, beriberi may develop.

MCCLELLAND, Cleveland.

SOCIAL SERVICE. EDMUND GILLET, Rev. méd.-sociale de l'enf. **1**:400 (Nov.-Dec.) 1933.

This is a plea for coordination among various ministerial departments and private agencies devoted to social betterment.

LESLIE, Evanston, Ill.

INFANTILE HOSPITALISM. D. ANGARANO, Pediatria **42**:490 (May 1) 1934.

Angarano calls attention to the continued high morbidity and mortality among nursing infants in institutions, in spite of the advancement made in the field of infant feeding and infant hygiene. He discusses fully the various means usually adopted to attempt to reduce the morbidity and mortality rates among hospitalized infants, including complete isolation, prophylactic measures, personal and general education and the application of modern hygienic methods. His conclusions are that the real causes of hospitalism are the great frequency of infections developing secondary to other diseases as a result of the reduced general resistance of the patient.

SIGNORELLI, New Orleans.

THE PEDIATRIC CLINIC. P. NOBÉCOURT, Arch. de pediat., Rio de Janeiro **6**:759 (May) 1934.

Professor Nobécourt reviews the work done at his Hôpital des Enfants Malades since the death of Professor Hutinel and discusses the measures necessary to establish an efficient children's service.

SANFORD, Chicago.

THE NEW LAW OF MINORS. E. BALLÓN, Bol. Inst. internac. am. de protec. a la infancia **7**:361 (April) 1934.

Ballón analyzes the life of children in all its aspects, in order to show the autonomy of a privative and characteristic law of minors radically different from the laws already existing and independent of criminal and civil law.

The matters especially corresponding to the law of minors are the juridical, medical, social, educational and familiar problems involving every child, from the time of conception to that of the coming of age, regardless of the state of the minor. The law of minors must also take into consideration the mother and father—the latter because of his obligation to feed, educate and direct his decendants.

This law outlines the work of the tutelage of minors. This shall be, in the first place, of a preventive nature; second, it shall provide for the minors according to their deficiencies, and, third, it shall reform or regenerate according to the circumstances in each case. And if all this is necessary in regard to normal children, it is all the more so in the case of abnormal ones.

The legal principles establishing the rights of children and making them effective shall be applied by organizations employing special exclusive procedures based on psychologic observation and confidential investigation instead of violence and publicity and applying educational procedures of revalidation instead of penalty.

Therefore the code for children which shall consecrate their rights shall fix the standards regulating their assistance by means of tutelar institutions, patronages, homes for observation, shelter and protection, education and reform and work and direction in a vocation and the readaptation of deserted, mentally deficient or antisocial children.

AUTHOR'S SUMMARY.

MOST COMMON LABORATORY PROCEDURES USED BY THE PEDIATRICIAN. EUGEN STRANSKY, Paidoterapia **13**:7 (May) 1934.

This is an excellent review of the most common laboratory procedures used by the pediatrician. Owing to the rapid development of all branches of medicine, many of these procedures are absolutely necessary for the diagnosis of many diseases and are a great help in the diagnosis of others. Stransky describes in detail the laboratory methods used in the most common bacteriologic, chemical, serologic, roentgen and microscopic procedures. The laboratory procedures must be used only in conjunction with the clinical findings and are not to be relied on solely.

HERRON, Spokane, Wash.

EFFECT OF INSTITUTIONAL TRAINING ON THE MORAL DEVELOPMENT OF WAYWARD GIRLS. ANNA GREGOR and ADELBERT GREGOR, Ztschr. f. Kinderforsch. **42**:89 and 139, 1933.

This is a detailed study of all the girls who were admitted to the Maria-Victoria Home in Rastatt. Every girl is carefully studied in regard to her past history, family conditions and character. The authors believe that the first impression concerning the character of the wayward girl is of great importance in establishing a prognosis. It appears that despite very poor home conditions and a rather lurid past, the results of institutional training were unusually good. More than 70 per cent of the girls admitted returned to a stable form of life and appeared to become relatively valuable members of society. The development of moral quality seemed to go hand in hand with the development of intelligence. The girls who returned to an immoral life were usually those who had entered the institution with an unusually bad past history.

REICHLE, Cleveland.

TYPE OF PHYSICAL BUILD IN THE ADOLESCENT. A. M. GESELEVITCH, Okhr. Zdor. Det. i Podr., no. 5-6, 1933, p. 53.

In the study of one thousand adolescents of both sexes, 3 per cent whose build presented a characteristic difference from the usual build seen in the two opposite types and the middle type were segregated. These 3 per cent were below normal in weight, had long narrow trunks, short lower extremities, a narrow chest and face, a long neck, narrow shoulders, anomalies of the teeth and palate and a radial type of wrist. Their bony development corresponded to their chronological age. Usually an anamnesis showed a family history of alcoholism or insanity. These children were usually the last-born in large families, and many of them had had rickets or contagious diseases. Children of this type showed a higher coefficient of susceptibility than the normal child.

SEMENENKO-MCKHANN, Boston.

EXCRETION OF THE ACTIVE PRINCIPLES OF ERGOT IN MILK. F. I. FOMIN, Vrach. delo **16**:663, 1933.

Fomin reports the results of his experiments on the excretion of the active principles of ergot in human milk and its effect on the new-born.

Properly controlled experiments were conducted on twenty-nine nursing mothers, and clinical observations were made on the corresponding new-born. The presence of the active principles of ergot in milk was determined by various methods: physical (quartz lamp), chemical and biologic.

The conclusions were:

1. The biologic method of determining the presence of the active principles of ergot in milk is the most satisfactory. 2. The active principles of ergot are excreted in human milk and were found to be present by the biologic assay method in 90 per cent of the cases studied. 3. The milk of nursing mothers receiving ergot had an untoward effect on the new-born, as was manifested by drowsiness, loss of weight, anorexia and vomiting. 4. The administration of ergot to the nursing mother should be avoided or conducted along with careful clinical supervision of the new-born.

BODER, Chicago.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

Cleveland, May 2-4, 1935

BORDEN S. VEEDER, M.D., *President, in the Chair*

First Session

Thursday Morning, May 2

CLINICAL APPLICATIONS OF THE LYOPHILE PROCESS. DR. JOSEPH J. STOKES JR., DR. A. MCGUINNESS (by invitation) and DR. S. MUDD (by invitation), Philadelphia.

We have previously (AM. J. DIS. CHILD. **48**:1428 [Dec.] 1934) described a method for the preservation of human serum, dry, in vacuum, without apparent loss of antibodies when kept at icebox temperature (Eagle, H.; Strauss, H., and Steiner, R.: *Am. J. Clin. Path.* **5**:173 [May] 1935). This method was perfected by Flosdorf, working with one of us in the department of bacteriology of the University of Pennsylvania. It was the culmination of work started by Ehrlich and to which Martin, Shackell, Sawyer, Elser and Reichel chiefly contributed. Its scope of usefulness has been enlarged to include various types of serums and other biologic materials.

One hundred and ninety-eight children exposed to measles (102 in their homes) were given an intramuscular injection of processed convalescent or pooled adult serum. The results have been entirely similar to those reported for prophylaxis with ordinary human serum not processed.

Seventy-four children exposed to chickenpox (14 in their homes) and given an injection as mentioned showed results similar to groups given an injection of ordinary fluid serum.

Ninety-three children exposed to scarlet fever (50 in their homes) received lyophile convalescent and pooled adult serum. In 2 children extremely mild scarlet fever developed. These had received, respectively, 15 and 20 cc. of convalescent lyophile serum.

Twelve children with moderate to severe scarlet fever were given an injection of from 40 to 60 cc. of lyophile convalescent serum, with rapid improvement.

In 40 children exposed to mumps (16 in their homes) and given an injection as mentioned, the disease did not develop; with 2 exceptions—a very mild case in which the condition was unilateral, with an incubation period of twenty-five days, and a typical case occurring thirty-five days after injection and with an incubation period of thirty-six days.

Lyophile serum from adults immunized against typhoid fever by means of typhoid vaccine was injected intramuscularly in the treatment of 5 children with typhoid fever. Two children were practically moribund at the time of injection and died. In the other 3 cases the results appeared to be favorable.

Lyophile serum from persons recently convalescent from erysipelas was used for the treatment of 1 child with the disease. Rapid improvement occurred.

Lyophile serum from an adult immunized against Pneumococcus types I and II by means of Felton's carbohydrate antigen was injected intramuscularly into 1 patient with pneumonia due to Pneumococcus type I with infection of the blood stream. The pneumonia and infection of the blood stream cleared within thirty-six hours.

A recurrent epidemic of impetigo contagiosa in a maternity nursery was apparently interrupted by the use of 10 cc. of lyophile pooled adult serum injected intramuscularly into each new-born infant within twenty-four hours after birth.

In 7 "private" infants not given the injection but cared for by the same nurses and in the same nurseries the disease developed during the period of study.

Alternate patients with rheumatic fever admitted to the Children's Hospital have been receiving intramuscularly every four weeks 50 cc. of lyophile serum from adults over 35 years of age who have had no family history of rheumatic fever. These injections are given through the fall, winter and spring. The results so far have been favorable.

The lyophile process, when used in conjunction with such serum centers as those established in Chicago, Detroit, Milwaukee and Philadelphia, should greatly expand their usefulness for the study, prevention and treatment of infectious diseases and may make more feasible the establishment of similar centers in other communities.

DISCUSSION

Dr. James Dowling Trask, New Haven, Conn.: I should like to ask Dr. Stokes whether he has used the lyophile serum intravenously and, if so, whether it is necessary to be particular about the blood groups.

Dr. Joseph Stokes Jr., Philadelphia: In answer to Dr. Trask's question, we have not used lyophile serum extensively intravenously. As a rule, pooled adult serum can be used intravenously without a serious reaction, if given quite slowly. In these cases there has been no attempt to determine blood groups, and there have been no serious reactions. However, since we believe that it is possible for reactions to occur, it has been customary to give it intramuscularly. We think that intramuscular injections are probably just as valuable as intravenous injections for the treatment of infectious diseases.

Experimental Production in Monkeys of an Encephalomyelitis Accompanied by Myelin Destruction. Dr. Francis F. Schwentker (by invitation), Baltimore, and Dr. Thomas M. Rivers, New York.

The etiology of the encephalomyelitis accompanied by demyelinization that occasionally follows antirabic vaccination and certain acute infections, for example, vaccinia and measles, is unknown. The fact that large amounts of heterologous brain material are injected into patients undergoing antirabic vaccination has prompted the theory that this procedure is responsible in some manner for the changes in the central nervous system of those who become paralyzed. In order to test this theory experimentally 8 monkeys were given repeated intramuscular injections of aqueous emulsions and alcohol ether extracts of normal brain. The number of injections varied from 46 to 85. Paralysis developed in 7 of the 8 monkeys. The brain was the seat of definite pathologic changes accompanied by myelin destruction. Cultures of the involved brain remained sterile, and no transmissible agent was demonstrated. Eight control monkeys remained well; in the brains of 4 of these no lesions were observed.

DISCUSSION

Dr. Maurice Brodie, New York: I should like to ask Dr. Schwentker whether he believes that this experiment has any bearing on the paralytic myelitis which occurs in association with rabies. According to the statistics of the League of Nations and other data, there seems to be a higher incidence of paralysis in cases in which the antirabic treatment is in the form of active virus rather than inactivated vaccine. The vaccine made of active virus contains less brain material, whereas with the phenolized vaccine more brain tissue is present, since larger amounts are used. Yet the incidence of paralysis is decidedly lower with the phenolized vaccine.

Dr. James Dowling Trask, New Haven, Conn.: Did you find that both monkey and rabbit brains elicited the reaction that you described?

Dr. Francis F. Schwentker, Baltimore: We used only rabbit brain in this particular experiment. However, in another set of experiments we found that

rabbit brain under certain conditions, such as during autolysis, may become antigenic for the homologous animal.

I cannot answer Dr. Brodie's questions completely. We think that the process which goes on in the brain is not connected with allergy. We have found that in rabbits given injections of brain substance antibodies against brain tissue develop, and that the specificity of this reaction is dependent on the lipoid of the brain tissue. Since allergic reactions are dependent on proteins, it seems probable that allergy is not concerned here. Furthermore, we have never been able to demonstrate any skin reaction to brain tissue in the animals given the injections.

As Dr. Brodie has pointed out, the development of encephalomyelitis following antirabic vaccination is less frequent when formaldehydized suspensions of the cord are used. If the whole process is dependent on an antigen antibody reaction (I use these terms loosely here), the formaldehyde may alter the brain tissue in some manner to make it less antigenic.

ACTIVE IMMUNIZATION IN POLIOMYELITIS. DR. MAURICE BRODIE (by invitation), and DR. W. H. PARK (by invitation), New York.

The clinical problem in poliomyelitis is that of the prevention of paralysis. Although the administration of convalescent serum was gaining wider use from its first clinical use in 1911, controlled studies during the epidemic of 1931 failed to uphold its value. That still larger amounts of the serum or the use of a hyperimmune serum would hardly be more successful in preventing paralysis is indicated from studies on the pathogenesis of the disease.

The virus appears to enter by the nasopharynx and travel via the olfactory nerves to the central nervous system, where after coursing along the olfactory tracts it seems to become fixed to the nerve cells. Therefore, serum could scarcely reach the virus to stop its spread once the disease process had set in.

Therefore, we aim to prevent paralysis by active immunization. There is considerable evidence for the belief that with growth from childhood to adolescence there is a rated specific immunization of the population. But in this process some children contract paralysis, and so the purpose of active immunization is to obtain immunity with a perfectly safe antigen.

In the experimental animal—the Macacus rhesus monkey—of the various methods used, namely, subinfective doses of active virus, combinations of virus and serum and suspensions of virus inactivated with germicides, a formaldehydized inactivated vaccine seemed the most satisfactory. Accordingly the method was applied to children, and the children were given either one or two doses of 5 cc. The vaccine was made from a suspension of the spinal cord of monkeys infected with poliomyelitis inactivated with 0.1 per cent solution of formaldehyde for from eight to sixteen hours at incubator temperature, after which time the vaccine was no longer infective. The children were bled before and one month after immunization and were tested for antibody by determining whether or not their blood serums protected monkeys against various amounts of virus.

Of the 29 children tested, 4 of whom had no antibody, a few an appreciable amount and the remainder very slight amounts of antibody in the control period, 27 showed the development of antibody after the vaccine was given. One child who had no antibody in the control period and whose blood serum gave no evidence of antibody after a single dose of vaccine showed a response after a second inoculation. The antibody seems to develop within eight days. After five months, 21 were retested; 16 had maintained their antibody, 2 showed a decided drop and 3 had lost it. Six of the 16 were retested after eight months and have still had appreciable antibody, whereas 1 had decidedly less.

Up to the present, more than 1,500 children have been vaccinated for controlled studies, and only 3 or 4 showed generalized reactions, while a local reaction consisting of induration occurred in about one third of those vaccinated.

It was pointed out that only controlled studies during an epidemic and the administration of the vaccine to large groups of children under controlled conditions could determine its value.

DISCUSSION

Dr. Harold K. Faber, San Francisco: This subject is so important that I should like to ask Dr. Brodie to clear up one point. It seems to be generally agreed that immunity to the virus diseases in general is produced only by active infection. The presence of neutralizing antibodies in the serum under natural circumstances merely reflects the past occurrence of infection. When such antibodies against the poliomyelitic virus are produced by artificial means, does it mean that actual infection has occurred, with the production of a genuine protection against future infection, or merely that a humoral response has been elicited that bears no certain or probable relationship to such protection? This subject is one on which Dr. Brodie has not touched. I know that he has done considerable experimental work on so-called tissue immunity as compared with humoral immunity, and I wonder if he would say a few words on whether the production of neutralizing substances in human beings by his method is evidence of a true protection against poliomyelitis.

Dr. Maurice Brodie, New York: The work with the elementary bodies in vaccinia and the work with rabies vaccines, also the work recently done with Rift Valley fever vaccine and the work with the yellow fever virus indicate that one can get an immunity with a virus which is inactive, provided that the germicide does not act longer than necessary to inactivate the virus. One cannot overtreat the virus. That has been demonstrated clearly in the case of vaccinia virus by Craigie, using elementary bodies treated with formaldehyde.

In other words, the virus may be inactivated to just the point where it fails to infect, but there may be a residuum of the virus which cannot be demonstrated.

In our own work, if we treat the virus of poliomyelitis with too much formaldehyde or if the process of inactivation is carried out too long, we reach the point where it is nonimmunologic. This may be due to the loss of the slight residuum of living virus necessary for immunizing. One requires a larger amount of germicidally treated, as compared with active, virus.

We were not able to immunize with small amounts of inactivated virus. We had to use large amounts; with the active virus of monkeys we could get equal immunity with about half the amount of active virus.

There is not much doubt but that one can immunize with inactivated virus. The question is whether it is actually dead and how long the immunity lasts. These points have not been settled. This immunity with inactivated virus may not last more than six months or a year. We have been able to show antibodies after eight months.

With poliomyelitis one may start antibody production, which in the majority of cases may be increased by exposure to the virus and subclinical infection. The person may be exposed to the virus within a few weeks or months after the immunization has been started, and this may add to the immunity.

The work of Paul and Trask and others has shown that a great deal of this virus is around and there is a great deal of exposure to it.

One has to remember one other point; that is that there are both humoral immunity and tissue immunity. We have been able to show that the cord of an animal that has recovered from the disease and is immune inactivates virus, whereas the spinal cords of normal monkeys do not, indicating that there is some change in the tissues after infection. One may not get the tissue change with inactivated virus. It is probable that with active virus one gets both forms of immunity. If with formaldehydized virus one gets no humoral immunity, the secretions of the nasopharynx may have enough antibodies to prevent the entrance of the virus from the nasopharynx. Thus, when the virus enters the nose the secretions may contain enough antibodies to neutralize it. If this fails and the virus gets to the central nervous system via the olfactory nerve if there is a tissue immunity in addition this will act as a second line of defense. Whether both mechanisms of defense or only one operate with the formaldehydized virus remains to be seen by experiment.

THE 1933 EPIDEMIC OF ENCEPHALITIS IN ST. LOUIS; CLINICAL SYMPTOMS AND SEQUELAE IN CHILDHOOD. DR. THEODORE C. HEMPELMANN, St. Louis.

The epidemic of encephalitis which occurred in St. Louis in 1933 was in many respects unique in this country. Epidemics of a somewhat similar clinical picture, however, have been reported from Japan and Australia.

The disease is apparently due to a specific virus and has been successfully transmitted to monkeys and certain strains of mice. Within a period of three weeks after the onset, the blood of persons who have recovered usually contains neutralizing substances against the virus, the latter being apparently absent from the blood of patients who have had lethargic (Ecomono) encephalitis, Japanese type B encephalitis or the Australian x-disease.

The incubation period in monkeys (after intracerebral inoculation) is usually from eight to fourteen days, in mice about five days and in human beings contracting the disease probably between nine and fourteen days.

The pathologic changes consist of intense congestion of the cerebral capillaries; perivascular cuffing with lymphocytes and nerve cell degeneration. About one third of the patients who came to autopsy showed inflammatory changes in the kidney and occasional nuclear inclusions in this organ.

The disease was much commoner in older persons, only about 12 per cent of the patients being children. The general mortality rate in 1,104 cases was 20 per cent, but in children under 15 years of age it was only 5 per cent.

The symptomatology in children was similar to that in adults, except that the disease was usually milder and more irregular.

Two phases of the invasive period could be distinguished, the first consisting of general systemic manifestations (chilly sensations, malaise, lassitude, influenza-like pains in the back, limbs and abdomen, moderate headache and, less frequently, photophobia, catarrhal conjunctivitis, sore throat or mild coryza). Accompanying this there is usually some degree of fever, which becomes one of the dominant characteristics of the disease during the second phase, when invasion of the central nervous system becomes evident.

Three types of the disease were observed, the first with encephalitis or meningeal symptoms at the onset, the second with a definite period of invasion preceding the encephalitic manifestations and the third mild or abortive.

The encephalitic symptoms consisted of an abrupt rise of temperature, headache, stiff neck, the Kernig sign, mental confusion, tremors, slurred speech and irregular neurologic signs. They were often accompanied by certain of the systemic manifestations already mentioned. The latter were most pronounced in the second type, prior to the onset of the meningeal symptoms. The height of the disease was reached within a day or two following the onset, and in most patients convalescence was well established within a week or ten days after admission to the hospital.

The most characteristic laboratory finding was a high cell count for the spinal fluid, the cells consisting mostly of mononuclears, with normal spinal fluid sugar.

Of 57 children examined more than one and one-half years after their illness, only 6 showed objective evidences of the disease, and some showed progression of the process, as evidenced by the development of new symptoms. The severest residual sign was mild hemiplegia associated with epilepsy, the other children exhibiting chiefly subjective symptoms, such as nervousness, irritability, lack of concentration and in a few instances transient, blurred or double vision.

DISCUSSION

DR. BRONSON CROTHERS, Boston: I wonder whether physicians make full use of psychologic procedures in cases in which cerebral injury is suspected. Dr. Elizabeth Lord at the Children's Hospital in Boston has shown that some children recover in the sense that they regain their previous level, but fail to maintain orderly mental growth.

DISCUSSION

DR. HAROLD K. FABER, San Francisco: This subject is so important that I should like to ask Dr. Brodie to clear up one point. It seems to be generally agreed that immunity to the virus diseases in general is produced only by active infection. The presence of neutralizing antibodies in the serum under natural circumstances merely reflects the past occurrence of infection. When such antibodies against the poliomyelitic virus are produced by artificial means, does it mean that actual infection has occurred, with the production of a genuine protection against future infection, or merely that a humoral response has been elicited that bears no certain or probable relationship to such protection? This subject is one on which Dr. Brodie has not touched. I know that he has done considerable experimental work on so-called tissue immunity as compared with humoral immunity, and I wonder if he would say a few words on whether the production of neutralizing substances in human beings by his method is evidence of a true protection against poliomyelitis.

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Three types of the disease were observed, the first with encephalitis or meningeal symptoms at the onset, the second with a definite period of invasion preceding the encephalitic manifestations and the third mild or abortive.

The encephalitic symptoms consisted of an abrupt rise of temperature, headache, stiff neck, the Kernig sign, mental confusion, tremors, slurred speech and irregular neurologic signs. They were often accompanied by certain of the systemic manifestations already mentioned. The latter were most pronounced in the second type, prior to the onset of the meningeal symptoms. The height of the disease was reached within a day or two following the onset, and in most patients convalescence was well established within a week or ten days after admission to the hospital.

The most characteristic laboratory finding was a high cell count for the spinal fluid, the cells consisting mostly of mononuclears, with normal spinal fluid sugar.

Of 57 children examined more than one and one-half years after their illness, only 6 showed objective evidences of the disease, and some showed progression of the process, as evidenced by the development of new symptoms. The severest residual sign was mild hemiplegia associated with epilepsy, the other children exhibiting chiefly subjective symptoms, such as nervousness, irritability, lack of concentration and in a few instances transient, blurred or double vision.

DISCUSSION

DR. BRONSON CROTHERS, Boston: I wonder whether physicians make full use of psychologic procedures in cases in which cerebral injury is suspected. Dr. Elizabeth Lord at the Children's Hospital in Boston has shown that some children recover in the sense that they regain their previous level, but fail to maintain orderly mental growth.

This condition can be properly called arrest of development and seems to us a very real and entirely measurable phenomenon. I hope that Dr. Hempelmann will tell us about the ages of the children with encephalitis and will discuss the psychologic status.

Dr. Joseph Stokes Jr., Philadelphia: We have been interested in the preservation by the lyophil method of the serums of persons who have passed through epidemics of this type. We believe that the serums of persons who are convalescing from epidemic diseases of this type should be stored for assisting in the diagnosis of other similar epidemics by means of neutralization tests and for the determination of the prophylactic and therapeutic value of such serums.

Dr. James Dowling Trask, New Haven, Conn.: Were there any cases of the disease in which a normal spinal fluid was found?

Dr. Theodore C. Hempelmann, St. Louis: In answer to Dr. Crothers' question as to psychometric tests to see whether these children are advancing not only physically but mentally as well, this is a considerable task, which is planned for the future. So far no comprehensive studies of that nature have been made. This is the first examination in which any of the persons affected have been examined by a special committee. Those who show abnormalities of any sort are to be examined more completely by the committee of neurologists, internists and pediatricians, and it is hoped that then we can get some careful estimates of what is happening to the minds of these patients. In regard to younger children, it is, of course, important to see not only that they are where they were before the illness, but, as Dr. Crothers said, that they advance like a normal child. This is a matter that takes time and a long period of study.

The youngest child whom we saw, as I recall, was a baby of 4 months. That child has apparently developed normally. I mean by this that the child is learning to walk and talk at a normal age and to do the normal things for the age.

The youngest child with definite and marked residual signs is the one mentioned in the paper. This patient, who is now 4 years old, came into the hospital with a diagnosis of tuberculous meningitis, despite the fact that it was at the Isolation Hospital where most of the patients with encephalitis were and was seen by physicians familiar with the disease. The child was unconscious for weeks, then was spastic for many more weeks and did not talk for a period of several months. This child is now talking and walking, but has a definite, although mild, hemiplegia, as well as several epileptic attacks a day.

Dr. Stokes referred to the continued study of the virus and serum of these patients. That is going on all the time. Dr. Muckenfuss has perhaps the best opportunity of studying the serum of convalescent patients because he is located in St. Louis. There are always many specimens of each serum being tested in his laboratory to determine the neutralizing properties of the serum against the virus. I believe that Dr. Armstrong of Washington and Dr. Webster of New York are carrying out similar investigations, so as time goes on unquestionably a great deal more will be learned about what happens to these persons and whether the blood continues to neutralize the virus.

Contacts in St. Louis have shown neutralizing bodies in a large percentage of cases, even when such persons had never had any evidence of the disease. If I remember correctly, about 20 per cent of the specimens of the blood of the population in general on which the Wassermann test was done as a routine have shown neutralizing bodies.

Dr. Trask asked about the occasional occurrence of normal spinal fluid. In a small but definite number of instances the spinal fluid showed a normal cell count at the first lumbar puncture. The symptoms were so typical of encephalitis, however, that the patients were regarded as suffering from the disease, and in consequence the spinal fluid was tapped again three days later. In almost all such cases the typical increase in cells had developed. That is, even though the first count was normal, it was not unusual to find perhaps 250 or 300 mononuclear cells at the second tap a few days later.

Second Session

Thursday Afternoon, May 2

SPLENOMEGALY IN CHILDREN WITH EARLY HEMATEMESIS. DR. RICHARD M. SMITH and DR. SIDNEY FARBER (by invitation), Boston.

The histories of 15 children with splenomegaly and early gastric hemorrhage are presented. The differentiation of this group of cases from similar ones in patients with splenomegaly is discussed on the basis of early hemorrhage, lack of anemia and leukopenia, the varying size of the spleen after hemorrhage and the nonprogressive character of the condition. Thrombophlebitis of the portal and splenic veins is the probable pathologic basis for the disease.

Splenectomy alone will not cure the condition or prevent subsequent hemorrhage, although it may furnish considerable relief by removing a large reservoir of blood. Some further operative procedure must be undertaken which will reduce the demand on the dilated esophageal and gastric vessels. Ligation of the coronary veins or some similar procedure may be effective in this regard.

Mesenteric thrombosis is a frequent complication and can in some instances, at least, be predicted on the basis of a study of the blood platelets.

DISCUSSION

DR. THOMAS B. COOLEY, Detroit: There is a great deal of misleading information in the literature as to what can be accomplished by splenectomy in these cases. I am glad that Dr. Smith has brought out the point that it is not a sure cure. In our experience, it has been far from curative. In fact, with a much more limited number of subjects than Dr. Smith has had we have not seen any patient definitely cured by splenectomy, contrary to some of the statements that one finds in the literature.

I am not sure that this particular group ought to be considered as a clinical entity. I should rather take the whole group of symptoms, including splenic anemia, the so-called first stage of Banti's disease, and put them all together under thrombosis of the splenic vein. It seems to me that in the present state of knowledge this would be more satisfactory than to try to separate them.

DR. KENNETH D. BLACKFAN, Boston: I think that the practice of separating clinical entities as different groups from the all-inclusive term Banti's disease, splenic thrombosis, etc., offers a larger opportunity for the eventual discovery of the underlying pathologic and etiologic cause. The group of cases which Dr. Smith has reported illustrates this point of view. By regarding them as a distinct group he has been able to outline a more reasonable plan of treatment and, at least, to derive some information of great prognostic value. In contrast to the clinical entity here described, there is another group of cases of splenomegaly and anemia, but with certain distinctive findings in the blood picture, in which splenectomy is of more lasting benefit. Undoubtedly other clinical entities will be separated out of the Banti group when a correlation of different clinical and laboratory features with the pathologic state is attempted. It will be of interest, as this group of cases which Dr. Smith has reported is not entirely uncommon, for him to enlarge somewhat on other forms of therapy than the simple removal of the spleen, which has not, as he has said, been of permanent value to children with this symptom complex.

DR. ISAAC A. ABT, Chicago: I did not understand whether any of these children had leukopenia.

DR. RICHARD M. SMITH, Boston: I shall answer Dr. Abt's question first. Except immediately following hemorrhage, when there might be temporary leukopenia or leukocytosis, these children, when in good health, had a blood picture perfectly normal in every respect.

I might discuss a little more in detail the question of the effect of splenomegaly. Of the 15 patients, 5 have not had their spleens removed. Three of those are

dead. Another has just had a recurrence of hemorrhage and will have the spleen removed as soon as she recovers from this particular attack. The other patient has had extensive recurring attacks of thrombosis. (A photograph of the collateral circulation was shown.) That child has not had a splenectomy because we believe that if the spleen were removed undoubtedly the procedure would stimulate still further the formation of thrombosis and she probably would die following the operation.

Ten of the patients have had splenectomies done, and 5 of those are alive. One of them was operated on only three months ago. She has had something like seven attacks of hematemesis. One of the patients has been well for five years. All the others have had recurrences of hemorrhage.

One of them, who had the vessels ligated in the gastrohepatic omentum from the cardiac to the pyloric end of the stomach and had one slight hemorrhage soon after operation, has been well for three years.

It is hoped that by ligating the vessels, either the coronary vein or the vessels in the gastrohepatic omentum, it may be possible to reduce the flow of blood at the point where the bleeding takes place, at the cardia either in the esophagus or in the stomach, and so reduce the number of hemorrhages. All the patients who have died have died of uncontrollable hemorrhage, with the exception of 3. One died of postoperative pneumonia, the only death following splenomegaly; another had hemorrhage and extensive thrombosis as well. A third had thrombosis and perforation of the intestine.

I think that the hope for cure in these patients or the prevention of recurring hemorrhages which is the cause of death lies in devising some operative procedure which will control the blood at the cardia.

RECURRENT VOMITING. DR. CHARLES HENDEE SMITH, New York.

Recurrent or cyclic vomiting is rarely seen in hospitals, in this country at least, but is one of the conditions which must be studied in private practice, since it occurs mainly in the children of the upper economic classes.

Its etiology has long been in dispute. Many observers have noted its occurrence in families in which several members have suffered from migraine or sick headache. This fact cannot be put aside as unimportant. But after ketosis was noted to be a constant accompaniment of the attacks it has been widely accepted as the cause of them. There are definite reasons to doubt this. Ketone bodies are sedative to the nervous system, as shown in the ketogenic diet used in treatment of epilepsy. In ketosis due to starvation or fever, somnolence is the main symptom; occasionally convulsions are seen, but vomiting is rare and not incessant. Induced ketosis in children susceptible to recurrent vomiting does not produce attacks as a rule. Cure of the ketosis by giving dextrose does not stop the vomiting, and the ketosis may spontaneously disappear before the vomiting ceases. It is said to precede vomiting in some cases, but the observations on this fact are few. The events which precipitate the attacks are admitted by all to be those acting on the nervous system, producing nervous excitement, fatigue or exhaustion, and are much the same as those causing migraine. Allergy is blamed for both recurrent vomiting and migraine, but the association is not proved and may be accidental. In an allergic person exposure to the sensitizing agent may precipitate an attack of migraine.

The association of sick headaches and recurrent vomiting in families is close and nearly constant. Of 41 families in which there were cases of recurrent vomiting, for which good histories could be obtained, all except 3 contained one or more victims of severe, prostrating headaches, with or without vomiting and visual disturbances. Mild or moderate headaches due to eyestrain, constipation or sinusitis are not included. In 8 families there were cases of recurrent vomiting in two generations. In 12 of the patients who had recurrent vomiting as children migraine or severe headaches developed after puberty.

The normal incidence of migraine is said to be about 5 per cent of the population, so it is to be expected that only 1 case could be found in three and one-

third generations in an average distribution. Other family histories taken with the same care show only an occasional case of headaches of a severe character or none. The hereditary nature of migraine is recognized by many writers on that subject. Many children with recurrent vomiting have headaches with the attack or show more or less typical migraine in adolescence. Many persons with migraine are prematurely gray. They are often subject to seasickness, car sickness or motor sickness. Several of my patients have shown the latter and have grown up to be gray in the late twenties.

The nature of migraine is unknown, and there are many theories concerning it. Eyestrain, allergy, appendicitis, duodenal stasis, pituitary congestion or dysfunction, obscure toxins, epilepsy and vasomotor disturbances are all advanced as causes. A "nerve storm" due to fatigue or excitement, causing a spasm of the cerebral vessels, is a possible mechanism. It is mere speculation to try to explain why a child should vomit from the same causes which produce headache in adults. How-

Recurrent Vomiting and Migraine in Families

Families Showing Association	Patients with Recurrent Vomiting	Patients in Whom Migraine Developed	Relatives with Recurrent Vomiting	Relatives with Migraine
19 in 2 generations	19	30	3	27
22 in 3 generations	22	3	3	48
4 in 4 generations	4	2	3	14
1 in 5 generations	1	1	1	8
	46	36	10*	97
No history of migraine obtainable	5	1		
No notes on history				
Old cases at Bellevue Hospital	7			
Patients seen in consultation	1			
History lost	1			
	60	37		
Source of cases				
Private patients	30			
Patients seen in consultation	9			
Patients at Bellevue Hospital	15			
Students of the staff	6			
Males 31				
Females 29	60			

* Mothers, 8; fathers, 1; cousin, 1.

ever, severe migraine in adults is accompanied by violent vomiting, often for several days, and children are known to vomit more easily than adults.

The test of treatment also points to similarity between recurrent vomiting and migraine. The method of treating the former in vogue at present is to attack the ketosis and dehydration and let the attack wear itself out. But sedatives have a prompt and beneficial effect which cannot be appreciated by those who have not tried them. Migraine may also be aborted by the administration of analgesics or sedatives, but these must be given early in the attack to have much effect.

The following plan, which I have used for more than ten years, shortens the attack of recurrent vomiting to a few hours in almost every instance. After the first vomiting a cleansing soap-suds enema is given. One hour later a full dose of sodium bromide is administered by rectum (about ½ grain per pound [0.3 Gm. per 0.5 kilogram]). Phenobarbital or amytal may be used. Dry toast or crackers are given one or two hours later; orange juice in small amounts is allowed by midafternoon and cereal for supper. If vomiting recurs, the bromide is repeated, or a full dose of codeine (1/80 grain per pound [0.008 Gm. per 0.5 kilogram]) is given hypodermically. No fluids are allowed until dry food has been retained for several hours. The parenteral administration of fluids is not necessary except in cases in which the condition has been neglected for several days.

The attacks may be prevented or made less frequent by avoiding nervous and physical fatigue, by extra rests, a full diet and careful bowel hygiene. They may recur in susceptible children up to puberty through the unavoidable stresses of life and are likely to be followed by attacks of migraine in adolescence.

DISCUSSION

DR. FRITZ B. TALBOT, Boston: I am much interested in Dr. Smith's paper. I would go one step further than he has gone. He warns the parents that the attacks may return. I think that the attacks can be prevented from returning by a very simple procedure. The one feature in common which he has not emphasized as strongly as the other feature of the condition in all these cases is pure body mechanics.

In my experience, by the correction of pure body mechanics the attacks in the majority of cases never recur, and if they recur they do not recur more than two times. It takes time to correct the body mechanics. Sometimes it is necessary to have long muscle training and so forth, and usually some sort of support to hold up the lower part of the abdomen is required.

DR. JOSEPH BRENNEMANN, Chicago: My chief qualification for discussing this paper is that I do not know anything about the subject. There is a great deal of confusion in my mind about it. I have been wondering whether the speaker regards recurrent vomiting and cyclic vomiting as synonymous. If not, I do not know exactly what recurrent vomiting is. One sees a great many children who vomit from many causes. I do not know whether one should call that recurrent vomiting. If so, it is frequent.

I think that recurrent and cyclic vomiting are commonly used as more or less synonymous terms. In that case, I can say that I saw one case recently, the first that I have seen in many years. Cyclic vomiting is extremely rare. John Howland had several cases of cyclic vomiting in his family. He was a physician who thought in terms of biochemistry and metabolism. He studied the cases carefully and reached the conclusion that the condition was a mystery. One of his children had one of these attacks at Strasbourg. Czerny questioned the existence of such an entity. As he watched that attack he admitted that there was such a condition.

Some one read a paper before the pediatric section of the American Medical Association in which he said that the symptomatology of cyclic vomiting was so well known that it was not necessary to state what it was. He added: "The following report is based on 27 cases seen within the last three years." I have never seen 27 cases of cyclic vomiting. To me cyclic vomiting is an entity. It begins in early childhood. The patients vomit without a fever for three or four days and in a month or two vomit again for the same length of time. They stop vomiting somewhere near puberty. I think that it is extremely difficult to differentiate between this entity and vomiting due to other causes or recurrent vomiting, whatever that may be.

I am not quite certain that I, due to my lack of knowledge and confusion, have been helped by the discussion in the last twenty minutes. That is not saying anything against the paper; it has simply increased my own confusion of mind. I think that if ten of us talked about this subject there might be nearly ten different interpretations.

DR. DEWITT H. SHERMAN, Buffalo: I have been very much interested in this condition for many years and believe that the fundamental underlying cause is an unstable nervous system, which reacts poorly to various contributing causes.

The commonest contributing cause of such an attack of vomiting is an infection, and the commonest site of the infection is the nasopharynx. Consequently in Rochester, N. Y., where so many tonsils and adenoids have been removed, the frequency of cases of recurrent vomiting should be decidedly reduced.

Fatigue and excitement have been the contributing cause in some of my cases. In 2 cases the condition was definitely due to eyestrain. I never have seen a case due to hypoglycemia. The only case that I have known of in which hypoglycemia

was proved to be the cause of attacks of cyclic vomiting was one described to me by Almsted of The Netherlands. By restriction of carbohydrates in the diet he was able to reduce the blood sugar and produce an attack.

In my experience, next to infections gastro-enteroptosis is a common cause of recurrent vomiting. Dr. Talbot designated this type of case as that due to faulty mechanics.

In those cases in which the condition is due to gastro-enteroptosis I have had dramatic results from the use of proper abdominal supports. In preventing attacks the belt is worn till physical training has produced proper posture and good muscular tone. The younger the child the more essential the support is, for the small child cannot be expected to always have in mind that he must stand properly.

I agree with Dr. Brennemann that one sees much less real cyclic vomiting than formerly; one reason is that at present children have, as a rule, more stable nervous systems, owing to more comprehensive feeding.

I am glad to hear that Dr. Smith uses not only the modern technic of treatment but also the good old-fashioned bromide to aid in shortening an attack.

Dr. S. G. Ross, Montreal, Canada: Dr. Smith has undoubtedly helped to separate one group of cases. However, one might question the remark that he made indicating that in so-called cases of cyclic vomiting which are due to hypoglycemia there is not, as a rule, much vomiting. I believe that this is frequently not the case; we have all seen the type of child with hypoglycemia who vomits continuously for one to two days. When the child receives dextrose it immediately stops vomiting; this is accompanied by a return of the blood sugar to normal levels.

While these cases may be much more infrequent than the cases that Dr. Smith has discussed, I think that they represent a definite clinical group and one that is difficult to distinguish from his type of case without the aid of the therapeutic administration of dextrose or examination of the blood sugar.

Dr. Franklin Paul Gengenbach, Denver: I should like to call attention to the fact that the allergists themselves seem to make a distinction between true recurrent vomiting or cyclic vomiting and the vomiting which is associated with gastro-intestinal allergy or atopy.

It is interesting how the discussion has suggested a group of possible predisposing factors. Dr. Smith said that recurrent vomiting occurs in a peculiar type of child. A "peculiar type of child" seems to be summed up by the points brought out by the discussion. Thus the child is often the linear type with poor body mechanics. He is apt to be the very nervous type, and not infrequently he is the allergic type. I may also add that he usually has poor elimination. Thus by correcting the poor body mechanics one may help to relieve the child's nervousness and improve elimination, after which, of course, the attacks should become fewer unless they also have an allergic background, which requires special treatment of its own.

Dr. Horton Casparis, Nashville, Tenn.: I have had 3 or 4 patients whose attacks of vomiting were definitely associated with the ingestion of certain foods. One child had his attacks only when he went to the circus. The excitement and nervous exhaustion were thought at that time to be the cause of the vomiting. He was found to be sensitive to peanuts. He ate them only when he went to the circus, and the family, who were told that this might be the cause of his attacks, refused to believe that the peanuts had anything to do with them. To prove that there was no association they gave him peanuts on two later occasions, and each time three or four days of vomiting followed.

Each of the patients just mentioned was found to be oversensitive to certain foods. All had attacks of vomiting lasting from twelve hours to three or four days following the ingestion of these foods. In every case there were several purposeful or accidental repetitions of the experiment, with the same results.

Still another child vomited for varying lengths of time after eating chocolate. As she approached puberty the attacks of vomiting stopped, but eating chocolate then was followed by so-called sick headache.

Of course this does not prove that allergy or oversensitiveness to food is the cause of recurrent vomiting. My experience suggests, however, that at least in some cases there is strong evidence that the ingestion of foods to which the patient is sensitive either is the trigger that sets off the attack or is the actual cause of the vomiting, which tends to continue as long as any of the food causing the attack remains in the intestinal tract.

DR. CHARLES HENDEE SMITH, New York: I am familiar with Dr. Talbot's paper on the relation of body mechanics to recurrent vomiting. In addition to the abdominal support it is to be noted that he stresses the importance of additional rest periods for these children. I wonder whether the rest is not largely responsible for some of the results that he obtained.

As a matter of fact, not all the children whom I have observed have had bad posture. Many of them are strong and well nourished with good body mechanics and not the linear type. If the attacks of vomiting are frequent and severe enough to affect the nutrition the posture is likely to be poor, as it is in many children, especially if they are undernourished.

I am sorry that I have not made myself clear to Dr. Brennemann. I have used recurrent vomiting and cyclic vomiting as more or less interchangeable terms. This is a real condition, as any one who has observed the attacks will testify. There is a literature of many articles describing it. I do not include the cases of children who vomit once or twice at the onset of an infection or cases of the type of nervous vomiting associated with nervous anorexia, but only those of children who vomit all food and liquid for at least one day. The condition is not very common in this country, as shown by the fact that I have collected only about 40 instances in twenty years in private and consultation practice, and there are but 15 authentic cases in the records of Bellevue Hospital in twenty-five years.

Tonsillectomy helps these patients when the cause of the attack is recurrent infection of the tonsils, but I do not believe that the tonsils are the source of all the attacks. Many of my patients have had recurrences of vomiting after tonsillectomy.

Dr. Ross is correct in holding that some children with recurrent vomiting have a low blood sugar level, perhaps lower than that of normal children in starvation. But several of our patients at Bellevue Hospital have had a blood sugar level no lower than 100 mg. per hundred cubic centimeters and have continued to vomit when the hypoglycemia was corrected with dextrose. The patients with spontaneous hypoglycemia whom we have observed have had convulsions and disturbed sensorium but have not vomited. I cannot believe that hypoglycemia is the cause of recurrent vomiting.

The relation to allergy is interesting and not yet entirely clear. I observed a boy who was sensitive to nuts, which gave him asthma but occasionally seemed to induce attacks of vomiting. Chocolate is also a definite cause of migraine in some persons. It has seemed to me that allergy may be merely one of the causes which excites an attack of recurrent vomiting in a child who is subject to both conditions. But in many of the family histories of my patients it has been impossible to find any allergy. I cannot agree with Balyeat, who has found allergy interchangeable with migraine.

I had hoped that there would be discussion of the treatment. I should like to stress the results of sedatives at the very onset of the symptoms. I can find no reference to them except in a few older textbooks. Dunn and also Rotch stated that chloral hydrate and bromides can be used if the attacks are protracted or severe. Koplik maintained that codeine in a full dose is the only treatment of value. I have used bromide by rectum on every attack I have observed for more than fifteen years. The dose must be a full one and if not efficacious should be repeated or supplemented with codeine. The vomiting stops in a few hours in most cases and never lasts more than one day, even in children who have usually vomited for from three to five days. The loss of weight is thus greatly reduced.

COAGULATION FACTORS OF THE BLOOD OF THE NEW-BORN. DR. HEYWORTH N. SANFORD, DR. ELEANOR I. LESLIE (by invitation) and DR. MARIAN M. CRANE (by invitation), Chicago.

The fibrinogen content of the blood of the new-born for the first ten days of life was estimated on natural plasma by direct measurement of the fibrin. The natural plasma was obtained from venous blood withdrawn in chilled oiled syringes and needles into paraffined tubes embedded in ice. The fibrin was estimated by direct weighing on a milligram scale and by the modified micro-Kjeldahl method of Koch and McMeekin. By the use of natural plasma the error caused by the drawing of fluid from the cells by oxalate or citrate was done away with.

Estimations were made on 131 new-born infants for varying times during the new-born period. It was found that the fibrinogen content of the blood of those infants who were not given a complementary feeding immediately after birth averaged between 0.04 and 0.06 Gm. per hundred cubic centimeters of plasma lower than those given a complementary feeding immediately after birth. This decrease, however, is well within normal limits, which were found to average 0.38 Gm. per hundred cubic centimeters of plasma, with variations between 0.22 and 0.67 Gm. There is commonly a rise in fibrin during the first three days of life, after which there is no constant change.

The prothrombin content of the blood of the new-born was studied by means of quantitative and qualitative estimations of the platelets. Natural venous plasma was used, and the platelets were estimated after centrifugating the plasma in ice to remove the cells. The plasma containing platelets only was further centrifugated in ice until the visible platelets had been removed. Estimations were made on 40 new-born infants during the first ten days of life.

Qualitatively, the number of platelets in the natural venous plasma of the new-born for the first ten days of life show practically no daily change, varying between 500,000 and 600,000.

In natural venous plasma the coagulation time increases to the fourth day and then falls below the time of the first twenty-four hour period. The platelet-free plasma represents plasma that microscopically contains no intact platelets. Changes in the coagulation values for this plasma must represent prothrombin obtained by the disintegration of platelets or is a measure of the qualitative value of the platelets. The coagulation time of this plasma is considerably longer than that of the natural plasma and increases until the fourth day, when it falls, paralleling that of the natural plasma.

Qualitatively, therefore, the platelets of the new-born show increased resistance to disintegration which increases until the fourth day of life and then decreases.

This increased resistance to disintegration is shown by the longer time necessary for the blood to clot and explains the increase in coagulation time observed in the blood of new-born infants during the first four days of life. Whether this increased resistance to disintegration is due to inherent properties of the platelets themselves or to some circulating antithrombin is not known. It appears, however, that qualitative estimations of the platelets of the blood of the new-born give a true index of the prothrombin value.

MICROCYTIC, HYPOCHROMIC ANEMIA WITH GASTRIC ANACIDITY IN INFANTS AND CHILDREN. DR. HAROLD K. FABER, DR. CAMILLE MERMOD (by invitation), DR. A. LAWRENCE GLEASON (by invitation) and DR. ROBERT P. WATKINS (by invitation), San Francisco.

Using the fractional method of gastric analysis after stimulation by histamine (0.01 mg. per kilogram of body weight) in a series of 9 children between 7 months and 2 years of age and in 1 child of 11 years, all with anemia of the nutritional type, marked defects in gastric secretion were found in all: Free hydrochloric acid showed a low level (in 5) or was absent (in 5); there were a low total acidity and a low volume. Prompt improvement in the blood occurred when adequate doses of ferric ammonium citrate were given. Before such treatment the

chief characteristics of the blood were: a slight to moderate reduction in the number of erythrocytes, predominant microcytosis (a low mean cell diameter, a shift of the Price-Jones curve to the left, a low mean corpuscular volume) and achromia; a marked reduction in hemoglobin (a low total reading, a low total amount per cell, a low concentration in relation to the cell volume), and absence of signs of increased hemolysis (normal or increased resistance to hypotonic salt solutions, a normal icterus index, normal reactions to the van den Bergh test). During the response to iron the blood showed: an increased number of erythrocytes; marked reticulocytosis, and an increase in the size of the red cells (a shift of the Price-Jones curve to the right, an increased mean cell diameter and mean cell volume), with transient macrocytosis, and an increase in the total amount of hemoglobin and in the concentration of hemoglobin in individual cells. After the initial response to iron, the morphologic picture of the blood approached but did not return completely to the normal picture, and the reticulocytosis and macrocytosis disappeared.

In the case of twin girls, both of whom at the age of 7½ months showed no free hydrochloric acid in the gastric contents, with a very low volume and total acidity and marked anemia, reexamination of gastric contents and blood seven years later showed that one had low normal figures for gastric acidity with a low volume and still detectable microcytosis (but normal erythrocyte and hemoglobin values), while the other showed marked subacidity and definite microcytic, hypochromic anemia.

While in all the cases reported the condition is to be regarded as definitely abnormal (particularly in those cases with complete absence of free acid), it is suggested that in infancy the low volume and acid production that is apparently usual at this age period tends toward the faulty absorption of iron and the production of mild grades of nutritional (iron-deficiency) anemia. Attention is called to the sharp drop in the hemoglobin and the smaller drop in the erythrocytes during the first year (after postnatal hemolysis is completed), which are regarded as normal phenomena but are followed during the ensuing years by a gradual rise in the total hemoglobin and in the red cell count. The severer cases of nutritional anemia may perhaps be regarded as exaggerations of a regular trend.

Attention is called to the close resemblance between the anemia described (which is the common nutritional anemia of childhood) and the microcytic, hypochromic anemia of adults (chiefly middle-aged women) that is also associated with achlorhydria. In respect to the morphologic picture and other hematologic data, in regard to the response to iron therapy and to the defect in gastric secretion the two conditions are indistinguishable. In the case of children (as shown by the data reported for the twins), the anacidity, unlike that in adults, and hence the tendency to anemia, is apparently not always permanent, although in some cases it may be.

DISCUSSION

Dr. Kenneth D. Blackfan, Boston: We have observed for some time, as Dr. Faber pointed out, the relationship of the acidity and volume in a patient with this condition. Particularly in patients with dietary anemia or with severe secondary anemia resulting from infection "functional" achlorhydria frequently occurs. I wonder whether Dr. Faber has observed in such children a relation in the gastric acidity from period to period, that is, in a case of achlorhydria no response to histamine and later, after improvement, a response to histamine.

One point of particular interest is the occurrence in infants of a severe macrocytic type of anemia. In one recent case of this type we found achlorhydria without a response to histamine. Even though the reticulocytes resulting from the use of liver extract parenterally were characteristic, we were unwilling to accept these findings as diagnostic of addisonian pernicious anemia until knowledge of such conditions in infancy might be more complete.

Dr. Barnet E. Bonar, Salt Lake City: I should like to ask Dr. Faber whether any studies of the blood were made at birth in connection with any of these children.

Dr. Thomas B. Cooley, Detroit: I should like to ask whether Dr. Faber has found the achlorhydria to be obstinate in the great proportion of cases. I inferred from what he said that he had. Our experience has been that while we have seen this condition temporarily in most of our patients it has disappeared in what one might call a fairly reasonable time.

We treat all our patients with liver and small doses of iron; we believe that they get well faster with such treatment, but I do not know whether it makes any difference with regard to the achlorhydria.

Dr. Harold K. Faber, San Francisco: Repeated examinations of the gastric contents have been made in only a few instances. In one instance, 3 examinations within a period of two weeks all showed complete absence of free acid. The twins, both of whom showed complete anacidity at the age of 7½ months, were reexamined seven years later, and one of them still had marked subacidity, while the other had what is probably to be regarded as low normal acidity. In children, therefore, defective secretion may persist for a long time, as it does in adults, but, on the other hand, recovery of secretion may sometimes occur.

The macrocytosis observed in several of our cases, to which Dr. Blackfan refers, has usually occurred during the first phase of response to iron, simultaneously with increase in reticulocytes. So far as we can tell, the macrocytes are actually reticulocytes; they have not suggested addisonian anemia to us, and other characteristics of the blood in these cases are unlike the changes seen in the latter condition. Some years ago, one of us reported a case of anemia with a high color index and gastric anacidity in an infant of 9 months, who responded to liver extract, in which the picture was much more like that of addisonian anemia than that in any of the present series, but I have never thought that the proofs were conclusive. Liver was not used in any form in any of the cases presented today. We have not followed any of the patients from the time of birth up to the time anemia began.

The Pathology of Steatorrhea. Dr. A. H. Parmelee (by invitation), Chicago.

This article will be published in full in a later issue of the American Journal of Diseases of Children.

Immunizing Effect of Placental Extract Following Oral Administration. Dr. C. F. McKhann, Dr. L. E. Eckles (by invitation) and Dr. J. A. V. Davies (by invitation), Boston.

Protein extracts composed of the globulins derived from the human placenta contain diphtheria and scarlet fever antitoxins and antibodies which neutralize the poliomyelitis virus and protect exposed, susceptible children against measles.

Virus antibodies, as exemplified by the substance neutralizing the poliomyelitis virus, are demonstrable in all the globulin fractions, whereas the antibodies active against scarlet fever and diphtheria toxins appear to be sharply localized in the pseudoglobulin fractions. The measles antibody appears to be as widely distributed as the poliomyelitis antibody.

The extracts can be prepared on a large scale and have been found useful in the prevention and modification of measles. More than 1,300 children have received injections of the material. A small percentage of patients who have received injections of the extracts have had moderately severe local or general reactions. It is believed that these reactions are due in part to the presence in certain of the preparations of a large molecule tissue protein.

Tests of the immunizing effect following the oral administration of placental extract were made.

Twenty-three patients with positive Dick reactions showed negative reactions to the Dick test following the oral administration of the specific extract in cold water on an empty stomach. The duration of the negative stage was variable, but was prolonged to as long as eighteen days if iced alkaline carbonated water was used as the vehicle.

Tests of placental extract by oral administration in the prevention or modification of measles suggest that placental extract given by mouth is also effective in this disease The oral administration of the extract has not been accompanied by reactions. Further investigations of the optimal time and the method of administration are necessary.

DISCUSSION

Dr. Joseph Stokes Jr., Philadelphia: In slight confirmation of the work reported by Dr. McKhann, we performed a few experiments with the feeding of antibodies. Three children were given convalescent scarlet fever serum by mouth, and we noted with repeated Dick tests the fading of positive reactions.

It seems to me that there must be considerable material wasted. I think that Dr. McKhann thinks the same.

I am interested in asking Dr. McKhann how much of the preparation is not absorbed, or whether he has any means of testing the quantity that may be absorbed.

Dr. Isaac Abt, Chicago: If this preparation blanches the eruption produced by the Dick test, why would it not also blanch the eruption of genuine scarlet fever in its incipiency?

Dr. Charles F. McKhann, Boston: In response to Dr. Stokes' question, we believe that when the material was given in plain ice water probably from a half to a third of it was absorbed. Probably more than that was absorbed when it was given in iced carbonated alkaline water.

By intramuscular injection from 5 to 10 cc. of placental extract is necessary to produce reversal of the Dick reaction in a child. By oral administration reversal was at times obtained with a dose of 10 cc. In other instances 18 cc. was required.

There were only 23 patients on whom this experiment was tried. That is hardly a large enough series to justify quantitative estimation of the results. Further studies are being made, and we are not only trying to determine how many skin test doses of Dick toxin may be neutralized in one area after the placental extract has been administered, but we also are bleeding the patients and titrating the antitoxin in the blood stream after giving the material by mouth. These observations should give some index as to the amount actually absorbed.

With regard to Dr. Abt's statement, we did not mention the use of this material in the therapy of scarlet fever. I showed some slides indicating that placental extract blanches scarlet fever rashes. It blanches them probably as effectively as convalescent serum and horse serum antitoxins.

We have been using placental extract in therapy by mouth in certain patients with scarlet fever, but the scarlet fever has been mild, and we are not in a position to draw conclusions from studies of the few patients to whom the extract has been given.

Third Session

Friday Morning, May 3

The Problem of Control of Endocrine Function. Prof. A. J. Carlson (by invitation), Chicago.

Control of the work of the endocrine glands may take place by the following factors: (1) true secretory nerves to the gland cells; (2) the vasomotor nerves to the glands, which control blood flow and thus indirectly control glandular activity, as in the case of the kidney; (3) chemical control, such as the activation of one gland by the hormones of another, by metabolites in general or by specific dietary factors.

It is not improbable that all these factors are involved, but some are more important than others. In regard to the secretory nerve control, the only proved

instance is that of the medulla of the adrenal glands and the output of epinephrine. It is not certain that all adrenal activity is stopped by section of the secretory nerves, but the secretion is decreased, and by stimulation of these nerves it is, conversely, increased.

Considerable work has been done to show a direct secretory nerve control of the thyroid gland. Various methods, including sectioning of the nerves to the thyroid in toxic goiter and estimations of the basal metabolic rate, have been used. The results have been inconclusive. This is also the situation in regard to the secretory innervation of the pituitary gland, the adrenal cortex and the islands of Langerhans.

In regard to direct hormonal control of one endocrine organ over another, our best evidence at present is the relation between the thyroid, the anterior lobe of the hypophysis and the gonads. Decrease in the thyroid hormone tends to impair the function of all the organs of the body, including the central nervous system. Within limits, the activity and life of the gonads is proportional to the thyroid activity. In a similar way, the anterior lobe of the hypophysis produces one or two hormones with specific action on the growth and activity of the gonads. Gonadal hormones in turn act on the anterior lobe of the hypophysis.

There has been a tendency to more or less identify the function of the endocrine glands with that of the sympathetic nervous system. This view is merely a working theory, except in the case of the adrenal medulla, which produces under sympathetic nerve control a sympatheticoneuritic hormone.

One may be justified in testing this theory on selected patients even in the absence of clear indication of results in experimental animals, provided, of course, that such experiments on man are made with the best control and follow-up methods obtainable on human material and that all results, both good and poor, are carefully and honestly recorded.

THE COMPOSITION OF GROWTH IN INFANTS. DR. S. Z. LEVINE, DR. M. A. WHEATLEY (by invitation) and DR. T. H. MCEACHERN (by invitation), Flushing, N. Y.

The most reliable clinical criterion for appraising the adequacy of an infant's diet is his gain in body weight, and its routine application in practice has given satisfaction. From a physiologic standpoint, however, this method of appraisal is open to the criticism that identical accretions in the total body weight may result from the deposition within the infantile organism of materials of different composition (protein, fat, glycogen, water, minerals).

A physiologic evaluation of the efficacy of an infant's diet requires, therefore, not only knowledge of the total gain in weight but also a precise estimate of the qualitative composition of the "growth quota." In the absence of direct chemical analyses of tissues of infants such an estimate can be obtained only by balance studies, embracing measurements of the total intake, the total output and the resultant body shifts of each of the dietary components. A program of this nature entails concurrent determinations of the gaseous, water and mineral exchanges of infants under controlled conditions of diet. Such studies are reported in this paper.

This report includes a brief description of the metabolic methods employed and the results secured in 3 normal infants from 4 to 9 months of age receiving diets of powdered milk, cane sugar and water in varying amounts. Five observations of twenty-four hours' duration were made while the infants were on adequate formulas as judged by current standards (approximately 110 calories, 150 cc. of fluid and 4.5 Gm. of protein per kilogram of body weight in twenty-four hours); one observation was made while the infants were on a submaintenance formula, and one while they were on a hypermaintenance diet. To insure metabolic equilibrium, a preliminary period of constant diet preceded all the observations.

The results may briefly be summarized as follows:

1. Water comprised a very labile fraction of the materials retained within the organism, the amounts varying enormously from day to day in the different infants

and even in the same infant on similar diets. On the other hand, the organic composition of the growth quota was maintained at a relatively fixed level under constant dietary conditions.

2. Variations in the caloric content of ingested milk formulas from submaintenance to hypermaintenance levels were found to be reflected chiefly in alterations of fat in the body depots, the reservoirs for protein and glycogen being limited in the infantile as well as the adult organism.

3. The diets customarily employed in practice permitted the laying down within the infantile organism of organic materials in proportions corresponding to the composition of body protoplasm (in terms of dry weight) as determined by chemical analyses reported in the literature. The deposition of materials of this character is presumably conducive to optimal growth.

4. The reliability of the observations was demonstrated by the similarity in the figures for the change in the total body weight as obtained by direct measurement with the balance and as calculated by algebraic summation of the increments made available for deposition in the body.

DISCUSSION

Dr. Fritz B. Talbot, Boston: This contribution is valuable and has a direct bearing on what I shall say later this morning.

I should like to have the members concentrate their attention on the last chart which was shown, illustrating what happens with a submaintenance diet. It shows that when there is a loss in weight, in the beginning, at least, the greater part of this loss is in the form of fat. That has a direct bearing on the interpretation of the figures for the basal metabolism and the results, in any case, in a person who is under the average weight.

Dr. Charles Hendee Smith, New York: I cannot resist the opportunity to call attention to a certain group of physicians who approach each new mother with the following statement: "Mother, do you want a large baby, a small baby or an average baby? We can make him any size you wish." I think that Dr. Levine has indicated that the big baby may be largely fat and water.

Dr. Bengt K. Hamilton, Chicago: In connection with the variations in weight which Dr. Levine mentioned, I would like to ask whether these were accompanied by variations in the minerals retained. If so, it would be interesting to know whether these minerals consisted of sodium, potassium or both.

Dr. Samuel Z. Levine, Flushing, N. Y.: In answer to Dr. Hamilton's question, the figures for the mineral balance found in this group of observations are not conclusive. There seemed to be wide fluctuations in the retention of the individual minerals—sodium, potassium and chlorine—irrespective of the retention of water.

We are repeating the observations in the room with constant temperature, using distilled water for the diet and analyzing, as have Dr. Hamilton and Dr. Swanson, not only the inorganic output by way of the urine and stools but also the mineral excretion by way of the skin and lungs. It is almost impossible to prevent infants from sweating visibly, especially when feeding. A definite but not excessive amount of minerals is lost by way of the skin and lungs.

The data are available, and we hope to correlate the water retention with the mineral retention at a later date.

Body Build and Disease in Children. Dr. Harry Bakwin (by invitation) and Dr. Ruth Morris Bakwin (by invitation), New York.

The external dimensions of children with three types of diseases (epilepsy, chorea and rheumatic heart disease) were compared with similar dimensions of a healthy control group from the same social environment. Curves for growth were constructed separately according to sex for the dimensions in the control group by

connecting average values calculated at yearly intervals. Standard deviations were computed for each average and curves plotted representing one standard deviation above and one standard deviation below the curve for the average.

The dimensions for each group with disease were then spotted at the appropriate ages on diagrams prepared as just described. The spots in the various areas on the diagrams were counted and the counts for the boys and the girls combined. The chi-square test was used as a measure of statistical reliability.

The three groups with diseases, when compared with the control group, showed statistically reliable deviations in the same direction: The face and its component parts and the shoulders and the hips (except in children with chorea) were narrow. No changes were found in the total body length, the sitting height, the span or the height of the upper part of the face. The weight was low in the group with chorea and cardiac disease and unchanged in the epileptic group.

The question whether the changes in body build in the children with epilepsy and rheumatic heart disease were present before these conditions developed or were effects of the disease is difficult to answer. In the case of an acute condition like chorea (only cases unassociated with those of cardiac disease were studied) there seems to be little doubt that the changes were present before the inception of the disease. It is suggested that the body configurational changes are outward, structural, measurable resultants of a trauma which at the same time has produced the more subtle physiologic changes on which predisposition to disease is based.

STANDARDS OF BASAL METABOLISM OF GIRLS (NEW DATA) AND THEIR USE IN CLINICAL PRACTICE. DR. FRITZ B. TALBOT, PROF. EDWIN B. WILSON (by invitation) and JANE WORCESTER (by invitation), Boston.

Previous basal metabolic standards for girls were supplemented and modified by standards determined on a new series of 87 normal girls. The metabolism of all the girls recorded in the literature was compared with the metabolism of Boston girls. The use of basal metabolic standards in clinical practice was briefly discussed.

DISCUSSION

DR. SAMUEL Z. LEVINE, Flushing, N. Y.: I merely wish to reiterate that we have had the same difficulty in appraising the value of basal metabolic determinations in children of abnormal configuration as Dr. Talbot had. Apparently any reliable standard suits the child of average body build. However, in our metabolic clinic we found that the obese child almost invariably gave basal metabolic figures between + 10 and + 15 per cent above all the standards at present in use, including the Aub-DuBois standards and Dr. Talbot's standards for height and weight.

We have been using, for clinical purposes, the Kessner-Knipping standards for girls and the Bierring standards for boys and have found, since adopting these, that the basal metabolic rate of obese children nearly always falls below + 10 per cent. We believe that for clinical purposes in routine basal metabolic examinations of persons of abnormal configuration these standards fall within a closer range than any that we had been using previously.

PROF. A. J. CARLSON, Chicago: How many tests were made on each individual child before the figure for the child was adopted? The reason I ask that question is because it seems to be more difficult to get the child to relax and into a real basal state than is the case with the adult. Dogs can be trained to relax far better than children. Can some of the difficulties here be ascribed to the difficulty of getting the child into the basal state? Would it be possible to get the basal state during the first or second hour of sleep? In that case the factor of relaxation would be eliminated.

DR. ALFRED H. WASHBURN, Denver: One point that Dr. Talbot brought out and one point that Dr. Levine brought out relate to experiences that we are

having in Denver in our research council. We have made about 450 basal metabolism determinations on 81 children, some of whom have been followed for approximately three years, with repeated tests every three months.

There is no question, I think, but that Dr. Talbot's point in regard to the wide variation that so many children show is correct. Apparently in our group the younger children seem to show even wider variation than the older ones, although we have few at present in the adolescent period. Most of them are between the ages of 2 and 10 years.

The point which Dr. Levine brought out is that most of the standards which have been in current use during the last decade undoubtedly tend to give too high a basal metabolic rate.

I hope that our first report will be ready some time this summer and that it will help perhaps, along with other recent reports, to furnish more reliable and normal standards to which the clinician can refer.

I do not mean to steal Dr. Talbot's thunder, but if he will forgive me I should like to refer to Dr. Carlson's remarks, because we have had some experience with the same children for a period of three years. It would appear, so far as we can see now, that the first two or three tests are apt to be so unreliable that we cannot use them. Most of the children, perhaps like dogs, after about three visits with us become accustomed to the workings and machinery, and after that we get apparently very reliable, even tests.

Dr. Fritz B. Talbot, Boston: In regard to Dr. Carlson's question, there is no doubt that some of our troubles are due to the methods used.

We had to decide first whether this would be a physiologic or clinical investigation. We needed so much material that we could not make it a physiologic investigation, as Dr. Washburn is undoubedly doing in his series of cases.

It is possible in the cot chamber to get a child to sleep, but it is not practicable with a portable apparatus. Our problem was to see whether we could not do something to make it easier for the clinician to make use of the basal metabolic test, and we did our work in the manner that the clinician would do it, taking all the precautions possible that we had previously taken in our earlier physiologic researches. We thought that what data we could give would then be valuable to the clinician. It is on that basis that this work is presented.

In regard to the fat child, I shall not have time to discuss that subject, but it is true that in the fat child the metabolism is higher when compared to the height than one would expect it to be in most instances. It depends on the composition of the body, the amount of fat relative to the amount of active tissue fat and water, as Dr. Levine suggested in his paper.

We have found that when the total calories for weight are considered fewer clinical mistakes are made in interpretation than with any other standard.

We have found also that in children with poor nutrition the standard of total calories for height usually is open to fewer clinical errors. But the main trouble is not that. No clinician would go into a patient's home, make a white cell count and, finding it to be 30,000, say, "Here is an appendix that is going to burst." He would, at least, feel the abdomen of the child.

What clinicians are doing is letting their technicians make a diagnosis in the laboratory without mixing up a bit of David Harum's horse sense. To have horse sense, one has to know how to look at the teeth of the horse and feel his hocks and withers. One has to "feel the hocks" of these children to get some sort of idea of their body composition, and one has to mix some horse sense with his clinical interpretations. If one does not mix that and take the trouble to learn a little of the physiologic background of this problem, and considers the determination merely as a mathematical test in which the standard can be applied, I advise such a person either to give up doing basal metabolic tests or to take the total calories for the height and the total calories for the weight, add them together, divide the sum by 2 and use that figure for comparison with the test case. That method is open to error, but the errors will not be as numerous as at present.

METHODOLOGY IN THE STUDY AND PRESENTATION OF PROBLEMS OF GROWTH AND DEVELOPMENT ESPECIALLY AS RELATED TO THE ADOLESCENT PERIOD. DR. WILLIAM PALMER LUCAS, DR. HELEN BRENTON PRYOR (by invitation), DR. HELEN MARIE JOHNSON (by invitation) and DR. ADELE S. JAFFA (by invitation), San Francisco.

In recent years an alteration has been going on in the methodology of sciences generally with the recognition of the importance of the quantitative point of view. There has been an invasion of statistical modes of thought and reasoning into all branches of science, both physical and biologic.

Philosophic-minded persons working in different branches of science began to conclude that groups of things, whether animate or inanimate, had certain characteristics as groups that were not expressed in individuals, no matter how typical. This principle held whether the groups were electrons or children. The statistical method furnishes a means of describing a series of observations as a group unit. Refinement of method has evolved formulas especially adopted to the analysis of biologic data.

The development of bacteriology during the last century served to focus the attention of physicians on the bacterial causes of disease and to warrant the assumption that microscopic organisms were the sole cause of disease. The methods used in bacteriology were nonstatistical in general.

As the study of disease progressed it became apparent that other factors than organisms were equally responsible for the production of disease.

As an illustration, the study of tuberculosis has shown that whereas a majority of adults in centers of population have been infected with tuberculosis, clinical tuberculosis develops in relatively few. It is now known that in addition to harboring of the organisms other factors are necessary to produce the disease. These may be related to the physical environment or may be more directly biologic, as the inherited constitution of the host.

The precise quantitative relations of the latter factors require a method of handling different from that employed in the science of bacteriology.

It remains for statistical methods of treating data to discover the relations of specific populations of human beings to specific groups of organisms. Age, sex and constitutional factors, as well as other group phenomena, can be analyzed only by the statistical method, which makes possible quantitative calculation of the results.

Todd stated that the adult form of man is the outcome of growth—enhanced, dwarfed, warped or mutilated by the adventures of life.

Both environment and diet can influence markedly the growing structures in childhood. The pediatrician who considers the positive side of building health prescribes an adequate and appropriate diet to promote optimal growth. The transverse diameters of the body are more affected by outside influences than the longitudinal, so that severe illness or inadequate diet are first reflected in measurements of width. The face has been shown to be very sensitive to disturbances in growth. Hellman pointed out that the transverse diameters of the face grow more rapidly during the first five years, while the vertical dimensions increase more rapidly after that. (Consequently an adolescent child with a relatively narrow face probably had a severe illness or nutritional disturbance in early life.)

Any study of growth requires measurements, the problems involved being how to measure and what to measure. Technics adopted by the International Anthropometric Agreement solve the first problem. Every investigator has his own special field of interest, and ours has been body build. Transverse diameters of the body determine body build and are gradually assuming much importance in the study of children.

We have used the term body build in the strict sense of type of bony framework designating large-boned and small-boned children. The state of nutrition has nothing to do with this definition of body build, which recognizes only the preponderance of the horizontal or the vertical dimensions.

We have anthropometric data on measurements of body build for 6,000 healthy, middle-class, American-born, white children from the San Francisco Bay region. They represent patients in private office practice, public school children and children seen in clinics of hospitals. All children seen in clinics for endocrine disorders and those suffering from serious or chronic illness were excluded. The socio-economic status of the group can be described only approximately, since no sociologic studies were made. It may be assumed that the children from private practice, comprising 49 per cent of the total number, came from financially secure homes, that those seen in the clinics of hospitals (17 per cent) came from an economic level below this, and that the public school children (34 per cent) could be divided between the two levels.

The statistical reduction of our data gives a norm for the general population of the geographic area under consideration, so that individuals or groups of individuals may be placed in respect to the amount and direction of deviation from the average.

Certain consistencies of physical characteristics stand out in the study of large numbers of children; thus, broad heads and broad faces are consistent with broad bodies, and vice versa.

The necessity of an accurate objective method for measuring body build is emphasized by the demonstration of definite relationships between body build and nutrition, body build and oxygen consumption or body build and the physiology of the gastro-intestinal tract. There is a presumptive relationship between body build and mental or personality make-up. And finally there are certain suggestive findings in the field of immunology which associate susceptibility to disease with general massiveness or the lack of it.

Many elaborate methods of classifying body build have been worked out, but the simple one of merely comparing the width of the body to the length appears to be adequate. The widest diameter of the crest of the pelvis divided by the standing height yields the width-length index which measures the relative breadth or body build of the child. This width-length index increases directly with the relative breadth of the child, since it expresses the simple relationship of each body to itself. Empirically it can be said that a low index means a slender child with small bones and a high index means a broad child with big bones.

Our study shows a continuity in the distribution of types of body build, with all variations from very slender to very broad builds, classified in terms of width-length indexes. The mean and median were almost identical, indicating a normal distribution curve for the indexes. The sigma or standard deviation is the most important constant, since it shows the amount of variation around the average. Standard deviations help to mark off zones of normality. The zone included between one standard deviation plus, and one standard deviation minus, the mean on a normal distribution curve takes in two thirds of the general population, leaving the other third to vary more than one standard deviation one sixth in each direction.

The word normal has ceased to mean average and has taken on rather the meaning of falling into certain ranges or zones of variation from the average, conveniently designated in terms of standard deviation.

The child whose physical traits all fall within the same zone, who varies from the average in the same direction and approximately the same amount for the different traits would be classified as normal whether he were much larger or much smaller than the average.

Comprehension of the whole child gives the physician a better perspective from which to observe disease processes. The correlation of morphology with physiology, immunology and psychology certainly gives a better comprehension of the whole child. Anthropometry as a basis of the study of morphology makes possible description in exact quantitative terms.

The significance of the material is determined by a combination of graphic, numerical and analytic methods. Graphic presentation has the great advantage of visualizing the distribution of cases throughout the entire range. The advantages of the frequency polygon are that it shows the distribution of cases, range, average

and skewness. If in each classification of the polygon both the number of cases and the percentage of the total are indicated it is possible to compare other sets of data containing a fewer or greater number of cases.

Chart 1 is a smoothed polygon showing the frequency distribution of 6,000 width-length indexes for both sexes for the ages of from 1 to 16 years. It demonstrates that these data fall into a normal distribution curve. The base line shows the range from an extremely narrow build (index 130) to an extremely broad build (index 190), with the majority of cases, in which the build was neither very broad nor very narrow, falling in the central range. The average or mean of the series cuts through the center of the distribution curve, showing no skewness in the material. The sigma scale marks the mathematical proportions of the surface area of the distribution curve. Between the ordinates 1 sigma + and 1 sigma —, are found 66⅔ per cent of the total population. In this series sigma = 7.23. Consequently one finds that two thirds of the 6,000 children were within 7 per cent broader and 7 per cent narrower than the mean width-length index 162.8. Also, only half the remainder, or 16 per cent, varied more than 7 per cent broader, while the other 16 per cent were more than 7 per cent narrower than the average.

Classification of children into linear or lateral types may be done on a basis of the sigma scale, since sigma is a mathematical constant. Any line of demarcation must be arbitrarily drawn, since there are no breaks in the even distribution curve. We have chosen the ordinates at 1½ sigma deviation to designate linear and lateral. This corresponds to roughly 10 per cent broader and 10 per cent narrower than the mean for the total population of 6,000 and varies somewhat at different age levels according to the sigmas.

We think that children who are more than 10 per cent narrower than the average may be considered the pure linear type and that they would have no lateral characteristics. Conversely, children more than 10 per cent broader than the average would be the pure lateral type. Between these extremes an intermediate type of children would partake of the characteristics of both extremes. The terms linear and lateral are loosely used to designate narrow or broad children, but if one draws an arbitrary line it would demarcate only extreme types.

Chart 2 gives the distribution of the width-length index of body build for adolescent girls and adolescent boys compared with the distribution for the total population. The curve for the boys is much skewed and shows a smaller range with a mean of 156.3, which is much narrower than the mean for the total population. The reason for this skewness is that adolescent boys grow in height much more rapidly than they spread, resulting in relatively narrow bodies and small indexes of build. Girls mature earlier and attain growth in height sooner than boys. Consequently, their indexes of body build are larger, and their range is more nearly that of the total population. The mean for the girls was 162.8, with a sigma of 9.81.

Chart 3 is a polygon showing the frequency distribution of the basal metabolic rates of children aged from 4 to 16 years. The rates were calculated on Benedict-Talbot norms when possible and on Benedict-Hendry-Baker or Aub-Dubois standards for oversized children. These data fall into a normal distribution curve, as may be expected of any biologic data in a sufficiently large series.

Chart 4 shows the distribution of the basal rates of adolescent boys and adolescent girls compared with those of the total population. The plots for boys and girls skew in opposite directions. Our data on younger children show progressively higher rates the younger the age. This is consistent with the rapid pulse rate and the higher body temperature in young children.

When the basal metabolic rates for all the ages are averaged according to width-length indexes, there is a definite trend toward high basal rates for narrow indexes and low basal rates for broad indexes (chart 5). There are both high and low rates for all the indexes, but when all the rates for a given body width were averaged the trend in relation to build was evidenced. By this method one group of slender children who had low basal rates were noticed especially, and further study showed that most of them were allergic.

Chart 6, a polygon showing the frequency of 50 psychologic behavior problems arranged according to width indexes, shows a high proportion of the children to be slenderly built. Their behavior problems were classified as follows:

1. (a) Impertinence, resistance, disobedience
   (b) Domination, bullying
2. (a) Dependence, whining or crying
   (b) Seclusiveness, day-dreaming
   (c) Shyness, feeling of inferiority, sensitiveness
3. Fears, night terrors
4. Temper tantrums
5. Thumb-sucking, masturbation, enuresis
6. Finicalness regarding food, anorexia, etc.
7. Hyperactivity, excitability, "nervousness"
8. Slowness, fatigue, etc.
9. Nonsocial behavior
10. School problems

Association Between Behavior Problems and Body Build *

	Index of Body Build	Type of Behavior Problem									
		1	2	3	4	5	6	7	8	9	10
Linear	Negative	36	20	12	14	9	6	19	5	11	12
Lateral	Positive	13	6	6	2	3	1	10	1	1	2

* Body build is expressed in terms of percentage deviation from the average.

Chart 7, a polygon illustrating the frequency distribution for the width-length indexes of 100 children with poliomyelitis, shows practically a normal distribution curve, with a mean of 161.7 and a range which closely follows that of the total population. This indicates that no special type of body build predominates among children who contract poliomyelitis. Other body measurements done on this group confirmed this finding.

Chart 8, a polygon showing the frequency distribution for 210 cases of tuberculosis in children aged from 2 to 16, is much skewed toward the narrow end of the base line. The mean width-length index for the group is 156.8, or 8.3 per cent narrower than the mean for the total group, and the range is much less. The mean width-length indexes for both sexes and for each age separately from 2 to 16 years are less than the means for the group of the total population corresponding in age and sex. This indicates that the 210 children with proved tuberculosis tended consistently to be of linear type of body build. Other body measurements on this group showed narrower faces, narrower heads and smaller interpupillary spaces than those of the general population. These measurements tend to confirm the theory that a linear type of body build is found in tuberculous children.

Charts 9 and 10 show the figures for mortality from tuberculosis for the United States, for California and for San Francisco; all show a sharp upturn at the adolescent period. This means that figures for morbidity would have the same trend a little earlier. The importance of tuberculosis as a problem of the adolescent period should be stressed.

Chart 11 shows sex differences in mortality from tuberculosis.

Chart 12 is a summary of the differences between the linear and lateral types in anatomic, physiologic, psychologic and immunologic panels.

Chart 13 is a graphic representation of the relative influences of different environments by ages, following Perry.

DISCUSSION

HOWARD WHIPPLE GREEN, Secretary, Cleveland Health Council: I take great pleasure in discussing this paper from the standpoint of the statistician rather than from that of the physician.

Dr. Lucas is to be congratulated on attempting this type of analysis, which is about the only type to be used to present the characteristics of a large group of children. He has demonstrated beyond the shadow of a doubt that our girls are broad and our boys are narrow.

In regard to the behavior problem, Dr. Lucas has demonstrated that the thin person presents a behavior problem more frequently than the broad one. I should like to see him separate his data by sex, showing the male behavior problem compared with the distribution of males, which, as I remember, was much skewed toward the narrow type, and the female behavior problem compared with the distribution of females. There is a possibility that more boys get into trouble than girls, therefore an analysis by sex should be made. The skew in the behavior may be due to the fact that there are many more boys than girls in the behavior sample.

The most pertinent of all the charts is that on tuberculosis. Because of the lower death rate among the boys of the adolescent age and the higher death rate among the girls of this age, one would expect to find that more children of the broader type have tuberculosis than those of the narrower type, simply because more girls seem to have it than boys. The charts show a very different picture, indicating that the narrow child is much more likely to become tuberculous than the broad child.

This curve also could be broken down by sexes. Each sex should then be compared with the normal distribution of that sex. I think that such a comparison would indicate a striking difference and one even greater than has already been demonstrated.

The charts also indicate to me that poliomyelitis affects our boys and girls in exactly the same manner.

I believe that these charts are very much worth while. I hope that Dr. Lucas will go back to San Francisco and do similar work on the Chinese. I should also like to see this method of analysis applied to the Negro, producing a normal distribution curve with which to compare the other curves. The method of presenting such a series of measurements *en masse* appears to me to be very worth while and a method that could be followed by other investigators in other sections of the country to great advantage with other groups of children—children of poor parents, children of very well-to-do parents and Negro children, as well as the native white children.

Dr. Lucas should be complimented on his presentation.

DR. HAROLD C. STUART, Boston: I am much interested in methods of presenting data for groups in such a way that one can extract useful information with regard to trends among different types of persons. I was interested in both Dr. Bakwin's presentation and that of Dr. Lucas from this point of view.

I should like to raise a question with regard to the difference which Dr. Lucas brought out in one chart comparing the build of boys and girls. Is this difference really an indication of the greater preponderance of the lateral type among boys than among girls, or is it rather an indication of the slower maturity of boys?

If you use chronological age for comparison, bring out the fact that boys are further removed from maturity than girls at any one particular age. Does not the chart rather suggest that in the latter stages of maturation the type is broadened? It seems to me that this material would have to be broken down in a different way to indicate whether or not boys are more lateral in type. One might possibly superimpose the distribution curve of boys on that of girls, with two years difference in the chronological age. I raise the question as to whether Dr. Lucas' figures do not demonstrate lack of maturity rather than difference in fundamental build.

PROF. A. J. CARLSON, Chicago: I do not know exactly what is implied by the lateral and linear type. Is it mainly adiposity? Of course, the size of the pelvis and the size of the shoulders, by and large, become a sexual factor. If the measurements are taken after the subjects have become problem children for a while and tubercular for a while, the question of adiposity may easily become secondary to that of disease, disturbance of digestion or disturbance of sleep. In other words, the type may be secondary to the problem or to the tubercular state.

DR. NORMAN C. WETZEL, Cleveland: The problem on which Dr. Lucas is working is a tremendous one and requires careful consideration of fundamental methods and objectives. He has asked on several occasions today whether such and such a thing might not be done "mathematically." The answer to that is: Everything he has described can, of course, be done if one wishes; what concerns me here, however, is the significance of the conclusions that can be drawn after the procedures that he suggests have been adopted. Dr. Weech proposes to deal with the purely statistical phases of work such as this, and it is therefore unnecessary for me to remark further on the histograms and the binomial curves which Dr. Lucas has shown.

The point that worries me most is the matter of creating indexes. It seems as though we in pediatrics, and hence, in applied physiology, are thereby allowing ourselves to be led into the very hazards that the engineers, astronomers and surveyors have always deliberately attempted to avoid. A similar problem arises in connection with the altogether unnecessary but nevertheless widely disseminated method of expressing metabolism in calories per square meter per day, for here is another example of "hit and miss" by which it is vainly hoped that "something" startling will be found when one thing is divided by another.

It should be most strongly emphasized that dividing one measurement, subject to error, by another likewise affected by error is in general disposed to increase the error of the result over that of either element; further, that the creation of an index in this way is tantamount to assuming that the reliability of the measurement in the numerator is exactly equal to that of the denominator. If this should not be the case, the error in the resulting index would be greater still. These difficulties can be easily avoided and just as much information can be obtained if the distribution curves are set up in terms of one variable alone, rather than as a distribution of an index which tends to be doubly loaded with error. Consequently, I should like to ask whether the distributions of width alone and height alone have been made and, if so, whether they, too, do not demonstrate the skew forms just as clearly as, if not more so than, the index curves that we have seen today.

DR. WILLIAM PALMER LUCAS, San Francisco: In regard to Dr. Stuart's question, the data on relative width were first studied by groups compiled according to age and sex, and these width-length indexes have been published. A histogram showing the distribution of the total data smooths into a perfect distribution curve. The group of adolescent boys shows a definite skew toward slender build, which becomes significant when compared to the total data. Using the curve for the total data as a background, it becomes possible to show where any particular defined group lies with reference to the total population.

Any individual child placed on the curve can therefore be seen in better perspective, since he is seen in respect to the amount and direction of his deviation from the average.

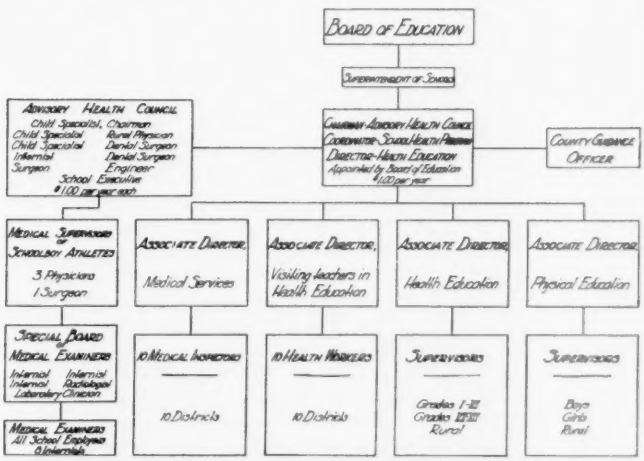
Answering Dr. Carlson's question, body build as we have defined it has nothing to do with nutrition. It is a question of the type of bony structure and does not consider the state of nutrition. In the study of large groups, of course, weight increases directly with width, and body build is a genetic factor.

Many investigators are going into growth and development problems, and all that we are seeking is an accurate graphic method of presentation.

The relative width of each child was calculated, and studies were made from the width-length indexes—not from the direct measurements.

MEDICAL PARTICIPATION IN A SCHOOL HEALTH PROGRAM. DR. GEORGE M. LYON, Huntington, W. Va.

"The physician, and particularly he who makes pediatrics his special study, is a pedagogue by profession. The question of school-house buildings and school room furniture, the structure of bench and table, the paper and type in the books, the number of school hours for the average child and the individual pupil, the



DEPARTMENT	MEDICAL INSPECTION	VISITING TEACHERS OF HEALTH EDUCATION	HEALTH EDUCATION	PHYSICAL EDUCATION
IN CHARGE	ASSOCIATE DIRECTOR	ASSOCIATE DIRECTOR	ASSOCIATE DIRECTOR	ASSOCIATE DIRECTOR
STAFF	10 INSPECTORS 10 DISTRICTS	10 VISITORS 10 DISTRICTS	3 SUPERVISORS GRADES I-VI GRADES VII-XII RURAL	3 SUPERVISORS BOYS GIRLS RURAL
ACTIVITY	Communicable disease control Sanitation and hygiene of the school and grounds Medical Athletics Daily inspection of health suspects No Health Examinations No Treatments No Immunizations	Communicable disease control District Administration School Health-Physician Program Medical Relief Social Service Liaison Agent Parent-Physician Parent-Clinic Visiting Teacher No personal relief nursing service No Immunizations	HEALTH PROTECTION PROGRAM - 6 POINTS Consultation service for teachers Materials, plans, classes, aids Health Education teachers pupils parents Publicity Speakers bureau Public Health Instruction Correlating the health program with regular curriculum	Program providing reasonable health implications Proper appreciation of rest as well as exercise of large muscles Competitive athletics of secondary importance Safety Education

Cabell County Program for Medical Participation in School Health Program.

number and length of recesses, the hours and duration of intervening meals, the alternation of mental and physical training, the age at which the average and the individual child should first be sent, have too long been decided by school boards consisting of coal merchants, carpenters, cheap printers and under-taught or overaged school mistresses. Not, however, by physicians."

In the nearly fifty years since Dr. Jacobi made these remarks in his presidential address before the first meeting of the American Pediatric Society in 1888, progress in the direction pointed out by him has not been as extensive as the

needs have warranted. In the earlier meetings of the Society much time was devoted to discussions of the important problem of school health protection. Kerley, Rotch, Edsall, Hamill, Holt, Abt, Caillé, Helmholz, Smith, Schroeder and Shaw have contributed actively in the discussions of this problem.

Impressed by the leadership of Dr. Hamill and by the varied influences of the Third White House Conference, our small group attempted a plan of medical participation in the school health program of a county free school system. Our experiment has been interesting and has many suggestive features.

In the fall of 1933, owing to a change in the basic school laws of the state of West Virginia and to a unique amendment limiting tax-levies which was put into effect at the same time, the board of education of Cabell County found themselves with no funds. They appealed to the county medical society for assistance in a crisis. A committee from the Cabell County Medical Society and the Huntington Dental Society was appointed to serve as an advisory health council to the board of education of Cabell County. It was their responsibility to reorganize and thereafter continuously supervise the county free school health protection and health education program. This offered real opportunity for medical participation in a school health program, and we attempted to employ the same fundamental principles that were applied by Dr. Vaughan in public health work in Detroit. The accompanying chart shows the administration setup for 1934-1935.

Features of the program besides medical participation were: (1) medical supervision of schoolboy athletes, (2) school medical inspection service (daily in urban schools), (3) physical examination of school employes by internists employed by the board of education, (4) appropriate supervision of medical relief in schools, (5) school health workers who were a combination of visiting teacher, social worker and health worker, (6) promotion of plan for immunization and welfare supervision in which schools supplied publicity and motivation and members of the medical society the administration of services in their private offices instead of at school, (7) health education as set forth in (*a*) the report of the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association and (*b*) publications on school health programs and their administration of the Third White House Conference and (8) a physical education program which provides proper health implications. Every phase of the program has contributed definitely in a positive manner. Some F.E.R.A. help was available in 1933-1934 but not in 1934-1935. The program cost the board of education only $1,000 in 1933-1934 and $6,000 in 1934-1935. This would have been impossible but for medical participation.

Health examinations, immunizations and other measures were not done by school physicians but by cooperating private physicians in their own offices at specially reduced fees ($1 for diphtheria toxoid, the Schick test, vaccination against smallpox, typhoid vaccine and dental health examination and $2 for health examination of a well child).

The program has resulted in many constructive attitudes, among which may be mentioned especially: (1) a greater community interest in and sympathy for public health and child welfare service; (2) a similar increased interest among the members of the medical and dental professions; (3) rapport, undreamed of before, between parents, teachers and physicians in problems of the control of communicable disease; (4) medical relief and immunization services *not* administered by the school from funds granted for educational purposes, and (5) an awakened interest and more sound attitude on the part of teachers with regard to health protection within the schools, with a similarly better attitude on their part in regard to what constitutes real health education endeavor and practice.

DISCUSSION

Dr. Richard M. Smith, Boston: What Dr. Lyon has said offers so many ramifications into the field of child health that one hesitates to start the discus-mendation of Dr. Lyon's presentation. He has called attention to a wide field for activity open to physicians who are particularly interested in the child. He sion. It seems, however, that one thing in particular should be said in com-

has developed a field of leadership which physicians have been too willing to resign to lay persons. If pediatricians ever expect to improve the health of the child of school age, and of course that leads into other ages as well, they can only do it by exerting positive leadership.

We have been too willing, I think, to simply give advice or to answer questions and have not been willing to take aggressive action. Dr. Lyon has demonstrated how in one community it has been possible for the physicians to exert a positive influence by being willing to take the initiative in attempting to organize a school health program. It seems to me that this principle can be applied in many other fields of child health and that the opportunity is very great. I believe that the responsibility rests on us to accept this obligation.

DR. LOUIS C. SCHROEDER, New York: It is not likely that in the fifty years of the existence of this Society there has been any one session at which the opening and closing papers so clearly demonstrated the depth and breadth of the interests which must enlist the attention of the members. Dr. Carlson's fascinating and instructive discussion of the problems underlying the control of glandular secretions represents the highest type of the scientific problems in pediatrics. Dr. Lyon's paper demonstrates beyond doubt what pediatricians can do to further the health of the child population.

As Dr. Carlson pointed out, it is not always possible, when dealing with such an abstruse problem as glandular control, to know in what direction one is headed, but with work such as Dr. Lyon has initiated in West Virginia the goal is clearly in sight, even if the means to attain it are not always so clear.

The goal is the betterment of school life for children by proper preventive measures, school sanitation and health education in its broadest phases.

It is not generally known how active the American Child Health Association has been in formulating and developing the problem of health education, and no one who desires to do what Dr. Lyon has done can afford to miss studying its numerous publications along these lines.

As a final word, may I express the wish that every county medical society will learn and profit by Dr. Lyon's splendid work in his home state.

DR. KENNETH D. BLACKFAN, Boston: A great many of us have not had the opportunity before to appreciate the remarkable influence on health education which Dr. Lyon has had in Huntington, W. Va.

I should like to ask what influence his advisory groups have had in regard to the subjects which are taught the child in the school in relation to health. I assume that in West Virginia the children are taught physiology, anatomy and hygiene. Has Dr. Lyon's group been able to control the subject matter covered by the school teachers themselves?

PROF. A. J. CARLSON, Chicago: There may be a wide gulf between the first and the last paper read this morning, but I do not think that there is such a wide gulf between the first and last speaker.

Of course, one must know what one is applying before one starts to apply it, and I am thoroughly in sympathy and understanding with Dr. Lyon in regard to the necessity that physicians take the lead in school health programs, both from the point of view of teaching and from that of the practical organization.

The unfortunate antagonism which has existed and still exists between the physician and the school boards' physicians and some of the teachers is going to require a long time to eradicate unless the physician takes such steps as Dr. Lyon has outlined. The physician knows more about the health problem than any other group in society, and he should be willing to distribute it. I am thinking not only from the point of view of the welfare of the child but also from that of the welfare of society as a whole and of the welfare of science, including medicine.

We cannot be many steps ahead of the common man and prosper. I look on this health program, the adult health education, as one of the imperative duties of whichever one among us who has the capacity to give that service. Not all of us have.

In my experience in connection with the health programs in schools, I have met a few teachers who will not cooperate. Those must be largely ignored, but the rank and file among them can be educated to see the value of such a program when it is put in the right light. I think that it is a very important line of work —as important as, if not more so than, giving one's time and effort free of charge to running clinics for the sick.

DR. GEORGE M. LYON, Huntington, W. Va.: We tried to start out rather simply in beginning our program. We were thoroughly imbued with Dr. Hamill's spirit when he visited us in West Virginia, and we were also very much attracted by Dr. Vaughan's application of medical participation in public health practice in Detroit. We were anxious to apply the same fundamental principles in a school health program.

The matter of supervision of the texts was put entirely in our hands, and it was our responsibility to select and choose. We had a difficult time doing it. During the last eighten months some fine little books have been prepared, which may be used in the elementary grades. To begin with, we concentrated our program on the first six grades.

Some fine literature on health instruction has been published recently, but we were not particularly sympathetic with most of the literature of that type up to that time. Our own state department of public health had put out a teachers' manual for public health education in which were listed twelve or fourteen health habits. We as pediatricians could not see how the health habits set out therein were particularly helpful toward letting the children know anything about health protection. Having the child go through a routine as a ritual, thinking that he had done his health duty for that day and that such a procedure was health protection, did not appeal to us.

We began writing to various authorities, asking what they considered were the fundamental health habits; so far we have not been able to determine them. Dr. Grulee told me that one of the committees of the American Academy of Pediatrics was still trying to find the fundamental health habits, if there be any such.

We tried to take the excellent work done by the Joint Committee on School Health Problems of the National Education Association and the American Medical Association and to use it as a "bible." We took the White House Conference publication on school health programs and the little blue White House pamphlet on school health administration and followed them. The teachers were told that they must not think of anything else except what was in these three publications. The advisory committee was permitted to do this, and the school administrator saw to it that the instructions were carried out.

We selected from the group of teachers those who were to be used as health education teachers or teacher-helpers. I was personally anxious not to have some of those from some of the larger centers who had been taught physical education and health education in the manner in which it is usually taught there. We wished to select some one who had a pleasant personality and who could take the books already referred to and develop from them what we thought were the proper attitudes about health direction.

I went through the literature on health education. I was disappointed to find so few of my friends of the American Pediatric Society actively participating in that field of writing. The majority of the writers were strangers to me.

So far as the large city is concerned, the program which we have attempted may possibly not be applicable. There may be many programs which may be fine as applied to the needs of the large cities which we cannot apply, but the program that we have attempted, I think, can be applied with benefit in a county with a population of approximately 100,000 which may have one or two fairly good-sized cities in it. The cost of such a program can be made very reasonable, as we have demonstrated. In this program only fundamentals and not "frills" were included.

The public school presents a different problem from the private school. My own mother has been in educational work since I was a child. She introduced into West Virginia in 1900 methods of primary instruction which in the light of modern educational practice are considered sound and acceptable. She has since 1909 been at the head of the Teachers' Training Department of the largest teacher's training college in the state. Because of this I have had an opportunity to see the school from the inside in a way that many pediatricians would not have. In an unconscious way, in this "model school," as it is called, a high type of health education and health protection is practiced. Every teacher is a social and health worker. She has almost daily contact with the home. She insists that parents keep children at home when they have a running nose or when they get up in the morning and vomit, are feverish and show other signs of illness. The parents generally utilize the local facilities for medical supervision in the hands of private physicians. There are no children from families of low socio-economic status. Health education and the development of good attitudes toward health protection are developed almost without effort. It is not necessary to have a medical staff for the control of communicable diseases. The parents and teachers work closely with the private physician. When one is dealing with the free school system the whole problem changes very much. The plan that we have tried is primarily applicable to a free school system. It is not meant in any way as a substitute for the truly constructive and fine school programs which have been worked out in many other places, particularly in private schools. It may be used where free school health programs of the usual inefficient misdirected type are in vogue.

I am not sure that the free school should undertake extensive health examination and other measures. An interesting point arose in this connection. We tried to carry out a plan for medical participation in a public health program along with this, so that all the immunizations and health examinations were done by private physicians in their own offices in a corollary type of program, separate entirely from the school. We thought that the school health program should not include immunization. One of the pediatricians on the Advisory Health Council was placed in charge as the pediatrician in charge of medical participation in the public health program. The school provides the publicity and the incentive to have this done, not the services of personal immunization.

The plan of the medical society provides for immunization against diphtheria, Schick tests, vaccination against smallpox and health examination of the well child. We have so much typhoid fever that we also include immunization against typhoid fever. Dental health examination is supplied by a similar plan of dental participation.

The schoolrooms have charts. Every time the child brings a slip from the physician showing that he has achieved one of the health protection aids the child is given a star after his name on his room chart. This in turn serves as a permanent record for the school. With one manipulation—the posting of the star to show the presentation of the physician's slip—the bookkeeping is all over.

We have been able to bring our program of immunization up to the level where 65 per cent of the children in the first grades are now immunized against diphtheria—a tremendous advance over the figures for three years ago. Next year we shall do the same with vaccination against smallpox. From now on we can concentrate in this respect on the children of the first and second grades and on the preschool children.

(To be Concluded)

Book Reviews

Comparability of Maternal Mortality Rates in the United States and Certain Foreign Countries. United States Department of Labor, Children's Bureau publication no. 229. By Elizabeth C. Tandy, D.Sc. Price, 5 cents. Pp. 24. Washington, D. C.: U. S. Government Printing Office, 1935.

This work reports a study conducted by the United States Department of Labor concerning the death rate in the United States due to or associated with pregnancy or childbirth, as compared with that in other countries. One thousand and seventy-three deaths were studied, of which 997 were assigned to the puerperal state and 76 to nonpuerperal causes. In 1927, the reports of 447 cases, including one of every combination or circumstance were sent abroad, and the condition was classified by sixteen countries as puerperal or nonpuerperal (Australia, Canada, Chile, Czechoslovakia, Denmark, England and Wales, Estonia, France, the Irish Free State, Northern Ireland, Italy, New Zealand, Norway, Scotland, Sweden, The Netherlands).

In Australia, The Netherlands, New Zealand and Scotland the assignments in use are similar to that in United States. In Denmark a larger number of deaths were assigned to the puerperal state; therefore the rate in the United States would be considerably higher. In Canada, Chile, Czechoslovakia, England and Wales, Estonia, France, the Irish Free State, Italy, Northern Ireland, Norway and Sweden a smaller number of deaths were assigned to the puerperal state; the death rate for the United States was somewhat lowered, but no matter which assignment is used, the United States stands high in regard to the maternal mortality rate.

Rates for the United States established in accordance with the assigned procedure of the respective countries are in every instance except in Scotland in excess of, and in five instances more than double, the official rates of the countries themselves.

Neither the definition of live births nor the incompleteness of the registration of births is of great importance in countries with comparable rates.

The death rate in the United States for puerperal sepsis is 25 per ten thousand.

Stammering and Allied Disorders. By C. S. Bluemel. Price, $2. Pp. 182. New York: The Macmillan Company, 1935.

This monograph, well fortified with reports of cases and bibliographic material, partially removes stammering from the field of psychology and places it in the realm of neurophysiology.

Bluemel refers to the experiments of Pavlov and others on the conditioned reflex and applies it to speech. Then he brings in the physiologic factor of inhibition and shows nicely the check that it exerts on conditioned reflexes and hereditary responses. He then carries this concept of conflict between the conditioned reflex of speech and inhibition through primary and secondary stammering.

Primary stammering is demonstrated as an immature conditioned reflex (a lack of sufficient positive reflex conditioning). Secondary stammering shows embarrassing associations negatively conditioning the subject not only to speech but to persons and situations.

In discussing the clinical side of the inhibitory influence Bluemel cites the check that inhibition exerts on conditional and, to a less extent, hereditary responses.

Various theories of stammering are appraised. The work of Travis, who believes in part that stammering is but a symptom of an extensive neurologic imbalance, is especially stressed.

Treatment is directed along the lines of the neurophysiology of speech. In a suitable environment application is made of the principles of reinforcement and unconditioning in an attempt to bring the stammerer back to the use of fluent speech.

Diseases of Children. By A. E. Garrod, O.M.; Frederick E. Batten, M.D.; Hugh Thursfield, D.M., and Donald Paterson, M.D. Third edition. Price, $10. Pp. 1151, with 277 illustrations. Baltimore: William Wood & Company, 1934.

This English textbook is a system condensed into one volume, written by many authors. The present edition is edited by Thursfield and Paterson.

The volume is well gotten out, and the black and white illustrations are excellent and well chosen. Not so much can be said for the two colored plates. This is the third edition, and while the volume is not amplified, it has been changed materially.

The introductory chapters are interesting; one is on heredity, and the other on immunity. These will be something rather new to American readers. Unlike similar works in the American literature, this text has no chapters on growth and nutrition. The chapter on artificial and breast feeding is much the same as previously. There are new chapters on blood transfusions and orthodontic treatment and on the new-born, as well as on diseases of the accessory nasal sinuses and the ear and on lipoidoses, acetonemia and other conditions. There is also a chapter on tuberculosis and a new chapter on allergy, which is rather short.

On the whole, the book is very interesting and should form a valuable edition to any library.

Healthy Babies Are Happy Babies. By Dr. Josephine Hemenway Kenyon. Price, $1.50. Pp. 321. Boston: Little, Brown & Company, 1934.

This handbook, written for mothers on the care of infants, is one of the best of its kind. Kenyon states that she has tried to anticipate the mother's questions and to inform her of the things she should know about the infant and herself as well, from pregnancy and through infancy until the child is 3 years old. The first chapter is devoted to a consideration of the mother's health and care during pregnancy and planning for the arrival of the infant. Each of the remaining chapters deals with a certain age period of infancy.

The book contains a great deal more than the usual advice about food and clothing for infants. There is a discussion of the child's physical development at each age period, his mental attainments and the problems of training and management that may arise. Moreover, the details of child care are described in such a way as to save the mother unnecessary work and time. Kenyon constantly reminds the mother about the proper care of herself during the care of the child. The outstanding feature of the book seems to be its wholesome attitude toward child psychology and preventive medicine in general. It can be highly recommended for mothers as an adjunct to the services of the family physician.

Therapeutisches Vademecum für die Kinderpraxis. By Prof. Dr. H. Kleinschmidt. Price, 6.60 marks. Pp. 215. Berlin: S. Karger, 1935.

This is the seventh edition of this small book devoted to the treatment of diseases of childhood. The therapeutics of practically all childhood disorders is discussed concisely. Considerable attention is given to the proper diet during illness. Medical management, physical-therapeutic measures and hygienic care are all given due consideration. There are a section on the preparation of foods for the well and sick child and also a list of children's institutions of various kinds.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.
Place: Basle, Switzerland. Time: Sept. 20-21, 1935.

FOREIGN

British Paediatric Association

President: Dr. Hugh Thursfield, 84, Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31 A, Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. R. C. Jewesbury, 5, Wimpole St., London, W. 1.
Secretary: Dr. Helen Mackay, 28, John St., London, W. C. 1.
Place: 1, Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Horton R. Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Place: Kansas City, Mo. Time: May 11-15, 1936.

American Academy of Pediatrics

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Region I. Place: Philadelphia. Time: Oct. 11-12, 1935.
Regions II and III. Place: Hotel Chase, St. Louis. Time: Nov. 18-19, 1935.
Region IV. Place: Seattle, with North Pacific Pediatric Society. Time: Aug. 9-10, 1935.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.
Place: St. Louis. Time: Sept. 30-Oct. 4, 1935.

American Pediatric Society

President: Dr. Fritz B. Talbot, 270 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

Canadian Society for the Study of Diseases of Children

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. C. F. McKhann, Children's Hospital, Boston.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Armin Rembe, Stimson Bldg., Seattle.
Secretary: Dr. Frank H. Douglass, 1227 Medical and Dental Bldg., Seattle.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.
Place: St. Louis. Time: Nov. 19-22, 1935.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. Morgan Smith, 625 Beech St., Little Rock.
Secretary: Dr. Madeline A. M. Melson, 2111 N. Spruce St., Little Rock.

GEORGIA PEDIATRIC SOCIETY

President: Dr. William Willis Anderson, 478 Peachtree St., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta, December 1935. Savannah, June 1936.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Louis H. Segar, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Charles James Bloom, 3439 Prytania St., New Orleans.
Secretary-Treasurer: Dr. J. A. Crawford, 834 Ryan St., Lake Charles.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.
Place: New York City. Time: April 27-29, 1936.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.
Place: Flint. Time: September 1935.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. R. E. Wilson, 205 S. Harvey St., Greenville.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. J. R. Ashe, 306 N. Tryon St., Charlotte.
Secretary: Dr. R. A. Moore, 306 N. Tryon St., Charlotte.
Place: Pinehurst. Time: May 6, 1936.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Francis T. O'Donnell, 345 North Main St., Wilkes-Barre.
Secretary: Dr. Theodore O. Elterich, 119 S. Highland Ave., Pittsburgh.
Place: Harrisburg. Time: Sept. 30-Oct. 3, 1935.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. William Weston Jr., 1428 Lady St., Columbia.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Memphis. Time: April 1936.

TEXAS PEDIATRIC SOCIETY

President: Dr. C. O. Terrell, 813 Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. P. McDowell, 142 W. York St., Norfolk.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. C. V. Mulligan, 17 Walmer Rd., N., Toronto.
Secretary: Dr. T. B. Verner, 170 St. George St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry M. Shapiro, 1882 Grand Concourse, New York.
Secretary: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. W. F. Watton, 240 Berkeley Pl., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. A. Levinson, 30 N. Michigan Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: College Hall, John B. Murphy Hospital. Time: Third Tuesday of each month.

DALLAS COUNTY PEDIATRIC SOCIETY

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

DETROIT PEDIATRIC SOCIETY

President: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

FULTON COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (ATLANTA, GA.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

HARRIS COUNTY PEDIATRIC SOCIETY

President: Dr. Byron P. York, 3820 Fannin St., Houston, Texas.
Secretary-Treasurer: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

KANSAS CITY (MISSOURI) PEDIATRIC SOCIETY

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

MEDICAL SOCIETY OF THE COUNTY OF KINGS AND THE ACADEMY OF MEDICINE OF BROOKLYN, PEDIATRIC SECTION

President: Dr. Charles F. Fisher, 736 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

MEDICAL SOCIETY OF THE COUNTY OF QUEENS, INC., SECTION ON PEDIATRICS

Chairman: Dr. Henry A. Reisman, 148, 88th Ave., Jamaica, L. I.
Secretary-Treasurer: Dr. Edith A. Mittell, 112 Queens Blvd., Forest Hills, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Béla Schick, 17 E. 84th St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.
Secretary: Dr. A. V. Stoesser, University Hospital, Minneapolis.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. George J. Feldstein, 3401 5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. W. A. McGee, 616 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Daniel Budson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: Nov. 22-23, 1935.

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